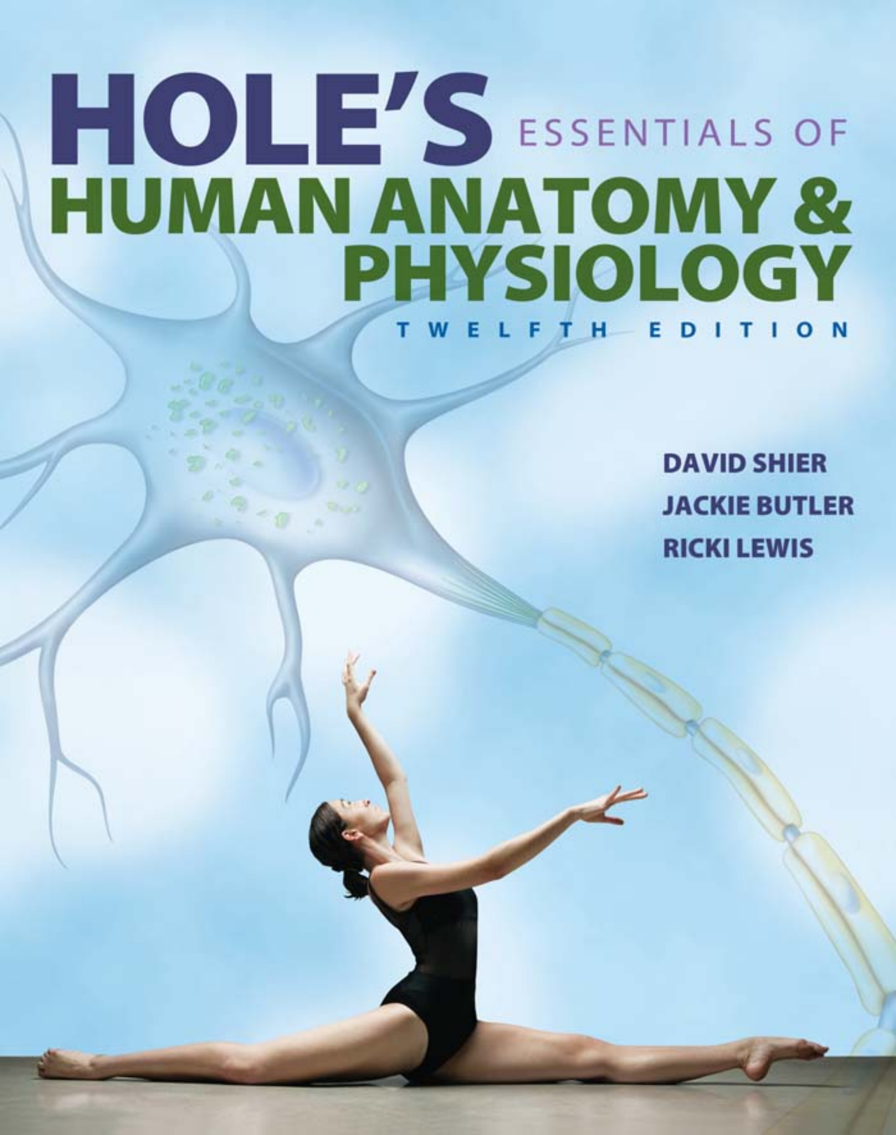
# HOLE'S ESSENTIALS OF HUMAN ANATOMY & PHYSIOLOGY

TWELFTH EDITION



DAVID SHIER
JACKIE BUTLER
RICKI LEWIS

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# HOLE'S
# ESSENTIALS OF
# HUMAN ANATOMY & PHYSIOLOGY

TWELFTH EDITION

**DAVID SHIER**
WASHTENAW COMMUNITY COLLEGE

**JACKIE BUTLER**
GRAYSON COLLEGE

**RICKI LEWIS**
ALBANY MEDICAL COLLEGE

Mc Graw Hill Education

HOLE'S ESSENTIALS OF HUMAN ANATOMY & PHYSIOLOGY, TWELFTH EDITION

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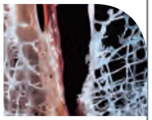

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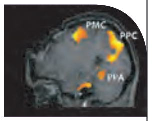

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# ABOUT THE AUTHORS

**DAVID SHIER** has more than thirty years of experience teaching anatomy and physiology, primarily to premedical, nursing, dental, and allied health students. He has effectively incorporated his extensive teaching experience into another student-friendly revision *of Hole's Essentials of Human Anatomy and Physiology* and *Hole's Human Anatomy and Physiology*. His interest in physiology and teaching began with a job as a research assistant at Harvard Medical School from 1976-1979. He completed his Ph.D. at the University of Michigan in 1984, and served on the faculty of the Medical College of Ohio from 1985-1989. He began teaching at Washtenaw Community College in 1990. David has recent experience in online course delivery, including recording lectures for so-called "flipped" classrooms. He has also been interested in the relationship between pedagogy and assessment, and the use of tools traditionally associated with assessment (e.g. lab quizzes) as pedagogical tools, often associated with group activities.

**JACKIE BUTLER**'s professional background includes work at the University of Texas Health Science Center conducting research about the genetics of bilateral retinoblastoma. She later worked at Houston's M. D. Anderson Hospital investigating remission in leukemia patients. A popular educator for more than thirty years at Grayson College, Jackie has taught microbiology and human anatomy and physiology for health science majors. Her experience and work with students of various educational backgrounds have contributed significantly to another revision of *Hole's Essentials of Human Anatomy and Physiology* and *Hole's Human Anatomy and Physiology*. Jackie Butler received her B.S. and M.S. degrees from Texas A&M University, focusing on microbiology, including courses in immunology and epidemiology.

**RICKI LEWIS**'s career communicating science began with earning a Ph.D. in Genetics from Indiana University in 1980. It quickly blossomed into writing for newspapers and magazines, and writing the introductory textbook *Life*. Since then she has taught a variety of life science courses and has authored the textbook *Human Genetics: Concepts and Applications* and books about gene therapy, stem cells, and scientific discovery. She is a genetic counselor for a large medical practice, teaches a graduate online course in "Genethics" at Albany Medical College, and writes for Medscape, the Multiple Sclerosis Discovery Forum, and Scientific American. Ricki writes the popular DNA Science blog at Public Library of Science and is a frequent public speaker.

MEET THE AUTHORS
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## DIGITAL AUTHORS

**LESLIE DAY** earned her B.S. in Exercise Physiology from UMass Lowell, an M.S. in Applied Anatomy & Physiology from Boston University, and a Ph.D. in Biology from Northeastern University with her research on the kinematics of locomotion. She currently works as an Assistant Clinical Professor in the Physical Therapy Department of Northeastern University with her main teaching role in Gross Anatomy and Neuroanatomy courses. Students enjoy her clinical teaching style and use of technology. She has received the teaching with technology award three times and in 2009 was awarded the Excellence in Teaching Award. She has been asked to speak about teaching with technology at national conferences and to give workshops on gross anatomy to a variety of professionals. She has also worked as a personal trainer both in local fitness facilities and at clients' homes, a strength and conditioning coach for collegiate athletic teams, an Assistant Groups Exercise Director for Healthworks and Group Exercise, and Fitness Director of three sites for Gold's Gym.

**JULIE PILCHER** began teaching during her graduate training in Biomedical Sciences at Wright State University, Dayton, Ohio. She found, to her surprise, that working as a teaching assistant held her interest more than her research. Upon completion of her Ph.D. in 1986, she embarked on her teaching career, working for many years as an adjunct in a variety of schools as she raised her four children. In 1998, she began full-time at the University of Southern Indiana, Evansville. Her work with McGraw-Hill began several years ago, doing reviews of textbook chapters and lab manuals. More recently, she has been involved in content development for LearnSmart. In her A&P course at USI, she has also used Connect and has enjoyed the challenge of writing some of her own assignments. When the opportunity arose to become more involved in the authoring of digital content for McGraw-Hill, she could not pass it up. Based on her own experience, students are using more and more online resources, and she is pleased to be part of that aspect of A&P education. .

# NEW TO THIS EDITION

## Global Changes

- Every piece of art updated to make it more vibrant, three-dimensional, and instructional.
- New digital authors created a seamless relationship between textbook and ancillaries/digital products in clever and engaging ways.
- Connect Question Bank has the same new art as the text and many new questions. Each Connect Question Bank chapter also includes an integrated question (a multi-step integration of chapter concepts).
- Career Corners, new to each chapter, introduce students to interesting career options.
- Each chapter ends with a list of online tools that students may use to study and master the concepts presented.

## Specific Changes At-a-Glance

| Chapter | Topic | Change |
|---|---|---|
| 1 | Scientific method | Chapter 1 introduces and Appendix B expands coverage |
| 1 | A&P updates | Rewritten with new examples |
| 1 | Body fluid compartments | New figure (1.4) |
| 1 | Homeostasis | Figure 1.8 (previously 1.4) simplified |
| 1 | Systems | More detailed introduction |
| 1 | Positional terms | Figure 1.14 redone with model |
| 1 | Body sections | Figure 1.15 sections now match sectional planes |
| 1 | Body regions | Use of terms “lateral,” “inguinal,” and “pubic” |
| 1 | Anatomical Plates | Redrawn for accuracy |
| 2 | Proteins | Levels of protein structure section rewritten |
| 2 | Atomic structure | Figures 2.4, 2.5, 2.7, now show corresponding IUPAC color of the element and number of protons, neutrons, and electrons |
| 2 | Polar molecules | Description reworded |
| 2 | Protein structure | Figure 2.18 better shows relationships among structural levels of a protein |
| 3 | Cell structure | Figure 3.2 added depth and vertical perspective; organelles more realistic |
| 3 | Mitochondria | New box on mitochondrial inheritance |
| 3 | Cilia | New box on cilia subtypes and related ciliopathies |
| 3 | Intracellular membranes | Figures 3.4, 3.5, 3.6, 3.10 have enlargement boxes that show phospholipid bilayers in membrane bounded organelles |
| 3 | Ion channels | Figure 3.14 now includes an ion channel |
| 3 | Phagocytosis | Figure 3.19 now has five steps |
| 3 | Cellular differentiation | Figure 3.23 simplified to better illustrate the roles of stem cells and progenitor cells |
| 4 | Metabolic reactions | New text art overview of metabolism |
| 4 | Metabolic pathways | New figure 4.8 shows a general metabolic pathway as a cycle, to lead into the specific example of citric acid cycle; reordered text to facilitate understanding |
| 4 | DNA structure | Figures 4.11 and 4.12 better depict relationship between bases and sugar-phosphate backbone |
| 4 | DNA versus RNA | Table 4.2 replaces figure 4.12 comparing DNA and RNA complementary base pairing |
| 4 | Complementary base pairing | Art for base pairs moved into figure 4.13, in context of transcription and translation |
| 4 | Transcription and translation | Figure 4.13 now shows translation beginning at the start codon |
| 4 | Translation | Figure 4.14 now shows translation beginning at the start codon and depicts correspondence between specific amino acids and specific codons |
| 5 | Tissue structure | All figures show more 3D idealized structure alongside a micrograph |
| 5 | Thin sections | Figure 5.1 is new and presents examples of how different cut sections would appear on a microscope slide |

*Continued next page—*

# NEW TO THIS EDITION

**Specific Changes At-a-Glance** *—Continued*

| Chapter | Topic | Change |
|---|---|---|
| 5 | Connective tissues | Material added regarding blood supply |
| 5 | Micrographs | New micrographs for figures 5.2, 5.3, 5.4, 5.11, 5.12, 5.14, 5.19, 5.22, 5.23, 5.24, and 5.25 |
| 6 | Skin functions | Material added to section on Vitamin D |
| 6 | Skin structure | Figure 6.1 adds hair bulge and new micrograph |
| 6 | Hair follicles | Material on the hair bulge added to text |
| 6 | Fingernails | Figure 6.4 redrawn and a new second view (orientation) added |
| 6 | Hair follicle | Figure 6.5 redrawn to include hair bulge, apocrine sweat gland and merocrine sweat gland |
| 6 | Sweat glands | Text describes merocrine (eccrine) and apocrine sweat glands |
| 6 | Wound healing | Figure 6.8 is new and shows the stages in healing of skin wounds |
| 7 | Bone marrow transplants | Rewritten box |
| 7 | Bone figures | Figures of the skeleton and of individual bones redrawn throughout |
| 7 | Skeletal structures | Table 7.2 "sulcus" added |
| 7 | Levers and movement | Figure 7.7 redrawn |
| 7 | Skull | Figures 7.10–7.16 have new coloring to clearly identify individual skull bones |
| 7 | Cleft palate | Rewritten box |
| 7 | Vertebrae | Wording added to section on the atlas |
| 7 | Vertebrae | Figures 7.18 and 7.19 redrawn |
| 7 | Atlas and axis | Figure 7.19 orientation arrows added |
| 7 | Scapula | Figure 7.22 redrawn to better correspond to location icon |
| 7 | Skeleton | Figures 7.23, 7.24, 7.25, 7.26, and 7.27, location icons added |
| 7 | Male and female skeletons | Table 7.3 rewritten |
| 7 | Hip bone | Figure 7.28 redrawn |
| 7 | Synovial joint | Figure 7.36 redrawn |
| 7 | Synovial joints | Rewritten text on joint capsule |
| 7 | Movements | Paragraphs added to clarify movement terms in context of anatomical position. Lateral flexion added |
| 7 | Movements | Figure 7.38 lateral flexion added |
| 8 | Muscle structure | Figure 8.1 redrawn to better show the relationship among epimysium, perimysium, and endomysium |
| 8 | Muscle fiber structure | Figure 8.4 redrawn to better show transverse tubules and to better illustrate relationship between thick and thin filaments |
| 8 | Neuromuscular junction | Section reorganized |
| 8 | Role of actin and myosin | Myosin heads distinguished from cross-bridges formed with actin |
| 9 | Contraction cycle | Figure redrawn to better separate continued contraction from relaxation |
| 8 | Mechanism of contraction | Figure redrawn to show pulling from both ends of sarcomere. Enlargement boxes added |
| 8 | Creatine phosphate | Figure 8.9 redrawn |
| 8 | Oxygen supply | Role of myoglobin rewritten |
| 8 | Oxygen debt and muscle fatigue | Formation of lactic acid, fate of lactate, and their roles in muscle fatigue rewritten |
| 8 | Motor units | Figure 8.13 redrawn to better isolate motor units |
| 8 | Agonists | Description of different muscle roles, such as agonist and antagonist, rewritten. New box on difference between agonist and prime mover |
| 8 | Muscle actions | Paragraphs added to clarify movement terms in context of anatomical position; paragraph added on multiple actions of certain muscles |
| 8 | Scalene muscles | Figures 8.17 and 8.19 now include scalenes |
| 8 | Muscles that move the head | Table 8.6 now includes scalenes and alternate role of muscles that aid in forceful inhalation |
| 8 | Muscles that move the arm | Paragraph added to clarify movements of flexion and extension of the shoulder |
| 8 | Muscle actions | Anatomical terms from chapter 1 are used throughout |
| 8 | Muscle illustrations | Figures redrawn throughout |
| 8 | Muscles of the pelvic floor | Text and figure 8.24 now include the central tendon |
| 9 | "Nerve impulse" and "Nerve cell" | New box clarifying usage |
| 9 | Synapse | New paragraph on the synapse added to introduction |

## Specific Changes At-a-Glance *—Continued*

| Chapter | Topic | Change |
|---|---|---|
| 9 | Action potential, impulse conduction, and synaptic transmission | Rewritten to clearly distinguish among these terms |
| 9 | Classification of neurons | Figure 9.7 now more diagrammatic |
| 9 | Facilitation | Explanation rewritten |
| 9 | Synapses | Figure 9.8 has a new part to show the schematic style of presenting neurons and synapses used throughout the chapter |
| 9 | Action potential | Figure 9.13 and the action potential introduction appear earlier in the chapter |
| 9 | Threshold | Figure 9.14 now includes a graph illustrating sub-threshold and threshold depolarization |
| 9 | Withdrawal reflex | Portions of this section rewritten |
| 9 | Brain | New brain figure |
| 9 | Brainstem | Figure 9.33 redrawn and locator icons added for anterior and posterior views |
| 9 | Cranial nerves | Figure 9.35 now has a (b) part illustrating the relationship of the nasal cavity, the olfactory nerve, and the olfactory bulb |
| 10 | Pain | Section now includes a reference to inhibition of pain pathways |
| 10 | Olfactory pathways | Limbic system added to discussion |
| 10 | Spiral organ | Figure 10.9 has improved drawings of innervation |
| 10 | Equilibrium | Figures 10.12 and 10.13 have improved location icons |
| 10 | Eye | Figures 10.14 and 10.17 now have location icons |
| 10 | Eye | FIgure 10.17 macula lutea added |
| 10 | Retina | Figure 10.22 new micrograph |
| 10 | Retinal neurons | Figures 10.21, 10.25, and 10.26 present same style for synapses as in chapter 9 |
| 11 | Target cells | Figure 11.1 redrawn to emphasize that hormones reach all cells, but only target cells respond |
| 11 | Pituitary gland | New text on intermediate lobe added to box |
| 11 | Pituitary hormones | New discussion of neurons that secrete pituitary hormones |
| 11 | Pituitary blood vessels | Redrawn presentation of hypophyseal portal system and associated vessels |
| 11 | Adrenal gland | Figure 11.13 redrawn to better show different zones and adrenal medulla |
| 11 | Effects of epinephrine and norepinephrine | Table 11.5 rewritten |
| 11 | Pancreas | Reworked description of the exocrine pancreas |
| 11 | Melatonin | Rewritten box |
| 12 | Blood cell counts | New box on variations in counts from different sources |
| 12 | Red blood cells | Figure 12.3 now shows cell membrane in section |
| 12 | Red blood cell life cycle | Figure 12.6 redrawn and legend brought up into text in numbered steps |
| 12 | White blood cell counts | Text and Table 12.1 include new values |
| 12 | Blood groups and transfusions | Substantial text rewrite |
| 12 | Rh incompatibility | Figure 12.19 redone |
| 13 | Overview of circulation | Figure 13.1 is new |
| 13 | Blood oxygenation | New terms used are “oxygen-rich” and “oxygen-poor” blood |
| 13 | Pericardial membranes | New figure with an enlargement box |
| 13 | Heart valves | Figure 13.6 adjusted for better orientation |
| 13 | Blood flow through the heart | Figure 13.7 modeled after 13.1 with only certain areas highlighted |
| 13 | Coronary vessels | Figure 13.9 redrawn |
| 13 | Cardiac cycle | Substantial rewrite |
| 13 | Cardiac muscle fibers | Detail added on intercalated discs |
| 13 | Electrocardiogram | Substantial rewrite, figure 13.14 has new art |
| 13 | Blood pressure | Figure 13.24 shows pulsatile pressure ending at capillaries |
| 13 | Arteries | Figures 13.27, 13.28, 13.29, 13.30, and 13.31 were redrawn for accuracy and consistency |
| 13 | Veins | Figures 13.32, 13.33, and 13.35 redrawn; figure 13.34, labels added |
| 14 | Overview of lymphatic system | Figure 14.1 is new and modeled after 13.1 for consistency |
| 14 | Lymphatic structures | Section 14.5, Lymph Nodes, is expanded to include MALT and titled Lymphatic Tissues and Lymphatic Organs |

# NEW TO THIS EDITION

## Specific Changes At-a-Glance *—Continued*

| Chapter | Topic | Change |
|---|---|---|
| 14 | Spleen | Figure 14.6 redrawn to better illustrate sinuses and red pulp |
| 14 | Lymphocytes and fetal development | Figure 14.13 redrawn to more accurately represent a fetal bone |
| 14 | Body defenses | Figure 14.11 is a new summary table |
| 14 | T and B cell activation | Figure 14.14 redrawn to include phagolysosome |
| 14 | Primary and secondary responses | Figure 14.17 redrawn with peak levels corresponding to text description |
| 14 | Allergic reactions | Section rewritten and expanded, and box on anaphylaxis made part of text |
| 15 | Mesentery | Figure 15.3 redrawn to better show mesentery |
| 15 | Movements through alimentary canal | Figure 15.4 redrawn to better show mucosa |
| 15 | Pancreas | Box on pancreatitis rewritten |
| 15 | Appendix | Update regarding role in maintaining gut microbiome |
| 15 | Duodenum | Figures 15.15 and 15.19 redrawn to show duodenum in its normal position |
| 15 | Liver | Figure 15.17 redrawn and combined with a new micrograph that corresponds better to art |
| 15 | Mesentery | Figure 15.21 has a new enlargement box detailing mesentery structure |
| 15 | Villus | Figure 15.24 redrawn to be consistent with figure 15.3 |
| 15 | Nutrition | Figure 15.33 now shows ChooseMyPlate.gov |
| 15 | Nutrients | Definition of nutrients added |
| 15 | Proteins | Wording added regarding protein digestion, absorption, and utilization |
| 15 | Vitamins | Table 15.9 has designations B7 and B9 added to vitamin names already listed |
| 16 | Organs of the respiratory system | Figure 16.1 and others redrawn, including lung anatomy |
| 16 | Pleural membranes | Figures 16.6, 16.7, and 16.11 redrawn, including color-coded representations |
| 16 | Inspiration | Scalenes added to text and figure 16.13 |
| 16 | Expiration | Figure 16.14 now includes elastic recoil of the lungs |
| 16 | Respiratory volumes and capacities | Table 16.2 reworded |
| 16 | Control of breathing | Figure 16.18 representation of cranial nerves redrawn |
| 16 | Diffusion across the respiratory membrane | Added to explanation of how partial pressures and diffusional gradients are related |
| 16 | Gas transport | Added a sentence explaining oxygen–binding capacity of hemoglobin |
| 16 | Gas transport | Added a paragraph explaining drop on $PO_2$ due to mixing with bronchial venous blood |
| 16 | Gas transport | Figures 16.20, 16.21, 16.22, and 16.23 redrawn with similar presentations |
| 17 | Location of the kidneys | Figure 17.1 redrawn, vertebrae labeled as markers |
| 17 | Kidney structure | Rewritten section on renal cortex and renal medulla |
| 17 | Nephrons | Explanation of functional units |
| 17 | Blood Supply of a nephron | Clarification regarding pressure in the peritubular capillaries |
| 17 | Structure of a nephron | Figure 17.6 has new part showing functional relationships |
| 17 | Overview of urinary system | Figure 17.7 is a new flow chart summarizing the urinary system |
| 17 | Filtration pressure and filtration rate | Sections rewritten |
| 17 | Urine formation | Figures 17.9, 17.13, 17.14, and 17.15 redrawn in same style to highlight relationships among processes in urine formation |
| 17 | Renin-angiotensin system | Figure 17.12 redrawn to better show the primary source of angiotensin converting enzyme |
| 18 | Body Fluids | Figure 18.1 redrawn with new schematic presentation |
| 18 | Transcellular fluid | Reworded description |
| 18 | Fluid movements | Figure 18.3 redrawn and legend elements labeled in figure |
| 18 | Balance | Significant rewording |
| 18 | Hydrogen ion concentration | Reworded to ensure that changes in pH are reinforced in terms of changes in hydrogen ion concentration |
| 18 | Respiratory alkalosis | Figure 18.13 redrawn to parallel related figures |
| 18 | Metabolic alkalosis | Figure 18.14 redrawn with new material |
| 19 | Semen | Expanded description of seminal fluid and prostate secretions |
| 19 | Sperm count | Table 19A values updated |
| 19 | Hormonal effects in males | Figure 19.6 relabeled to be consistent with figure 19.13 on hormonal effects in the female |

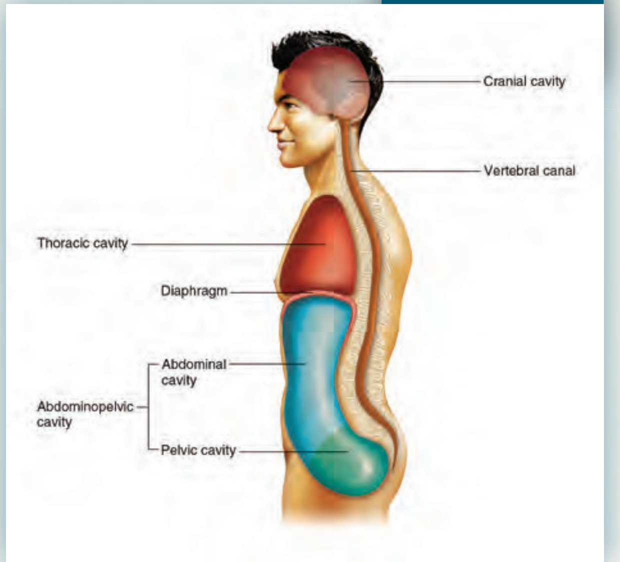
## Specific Changes At-a-Glance *—Continued*

| Chapter | Topic | Change |
|---|---|---|
| 19 | Female reproductive anatomy | Figure redrawn for accuracy |
| 19 | Oogenesis | Text rewritten to describe year-long maturation of a follicle |
| 19 | Ovarian cycle | Figure 19.9 redrawn to show stages of oogenesis as a timeline rather than cycle |
| 19 | Hormones of the ovarian cycle | Figure 19.14 redrawn to show more accurate hormone levels and only stages of follicle development in ovarian cycle |
| 19 | Menopause | Text reordered and rewritten for clarity |
| 19 | Contraceptives | Significant rewrite and additions |
| 20 | Fertilization | Section 20.2 retitled "Fertilization" and material on pregnancy moved to later section |
| 20 | Steps in fertilization | Text rewritten and figure 20.2 redrawn to more accurately show involvement of sperm cell membrane and enzymes |
| 20 | Pregnancy | Section 20.3 retitled "Pregnancy and the Prenatal Period" with text material added |
| 20 | Cleavage | Figure 20.3 redrawn for accuracy and consistency |
| 20 | Embryonic stage | Significantly reworked text with new material |
| 20 | Placenta | Figures 20.7, 20.8, 20.9, and 20.10 redrawn for consistency |
| 20 | Embryo | Figure 20.11 size expressed in millimeters |
| 20 | Prolactin | Material added to text |
| 20 | Fetal circulation | Terms "oxygen-poor blood" and "oxygen-rich blood" added to text and art |

# DYNAMIC NEW ART PROGRAM

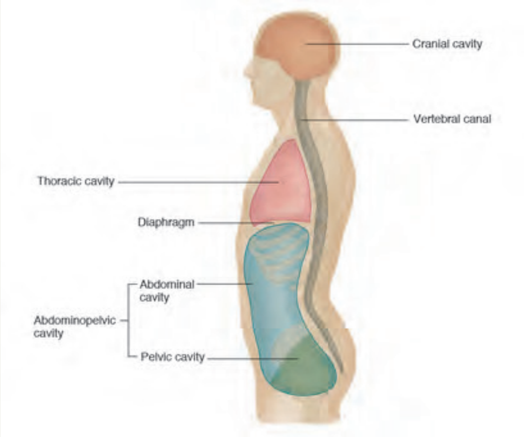
Every piece of art has been updated to make it more vibrant, three-dimensional, and instructional. The authors examined every piece of art to ensure it was engaging and accurate. The twelfth edition's art program will help students understand the key concepts of anatomy and physiology.

**12th Edition**



Cranial cavity
Vertebral canal
Thoracic cavity
Diaphragm
Abdominal cavity
Abdominopelvic cavity
Pelvic cavity

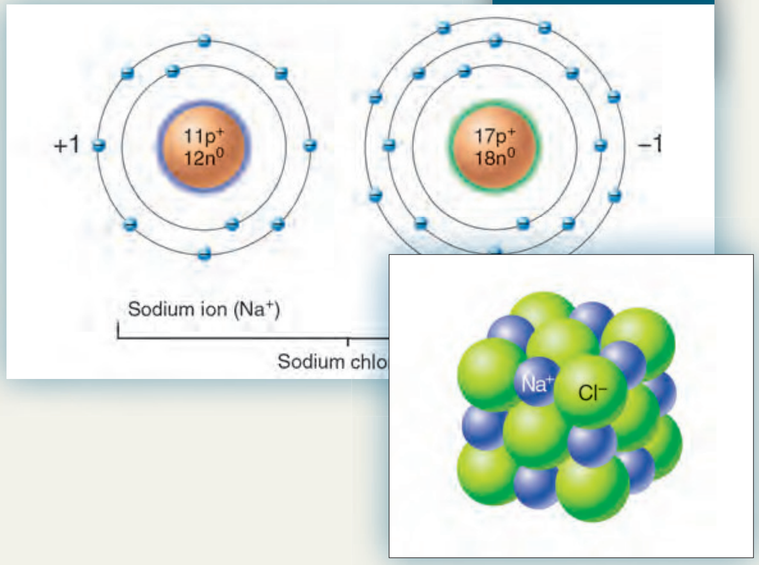
**11th Edition**



Cranial cavity
Vertebral canal
Thoracic cavity
Diaphragm
Abdominal cavity
Abdominopelvic cavity
Pelvic cavity

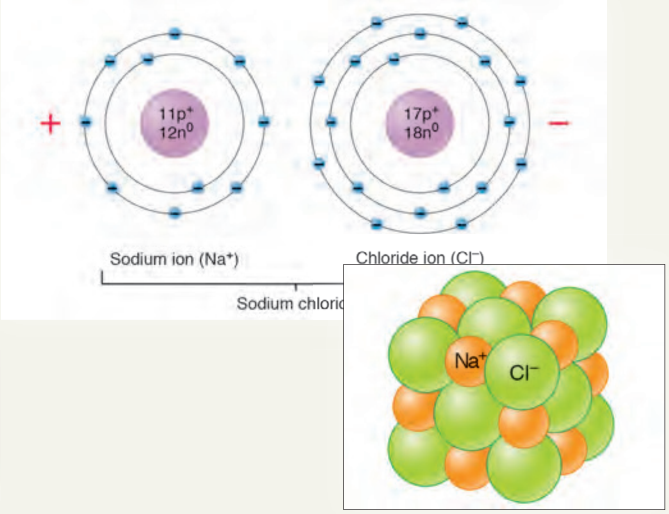
Realistic, three-dimensional figures provide depth and orientation.

**12th Edition**



+1
$11p^+$ $12n^0$
$17p^+$ $18n^0$
−1
Sodium ion ($Na^+$)
Sodium chlo
$Na^+$
$Cl^-$

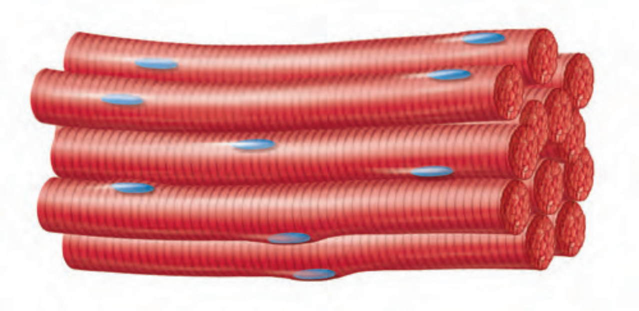
**11th Edition**



+
$11p^+$ $12n^0$
$17p^+$ $18n^0$
−
Sodium ion ($Na^+$)
Chloride ion ($Cl^-$)
Sodium chlori
$Na^+$
$Cl^-$

Colors highlighting atomic nuclei complement the atom colors in molecular models.

12th Edition



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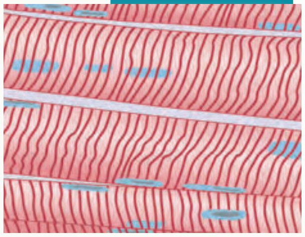
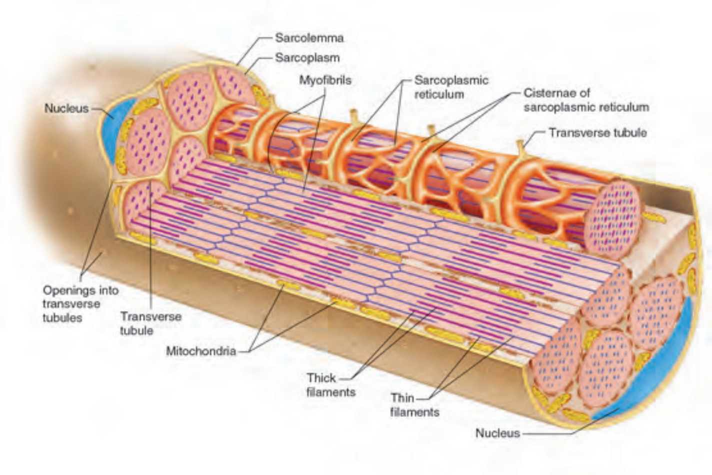
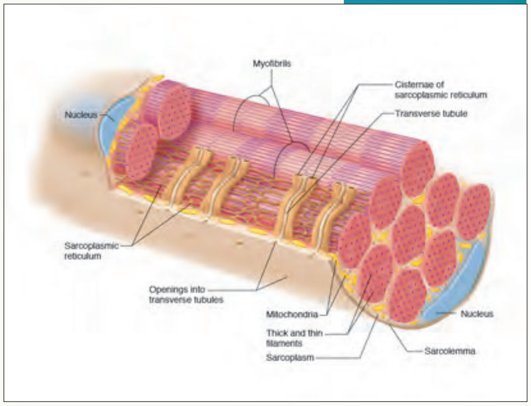


Line art for micrographs is three-dimensional to help students visualize more than just the flat microscopic sample.

12th Edition

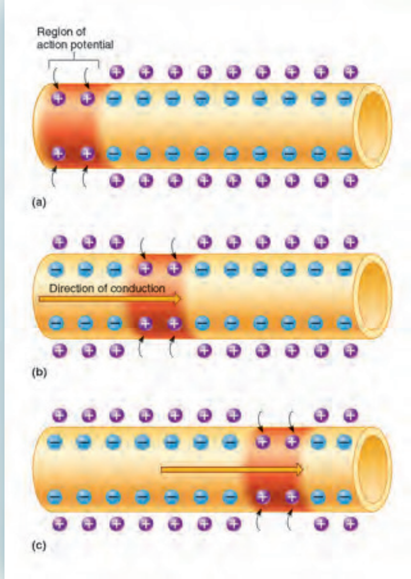

Sarcolemma
Sarcoplasm
Myofibrils
Sarcoplasmic reticulum
Cisternae of sarcoplasmic reticulum
Transverse tubule
Nucleus
Openings into transverse tubules
Transverse tubule
Mitochondria
Thick filaments
Thin filaments
Nucleus

11th Edition

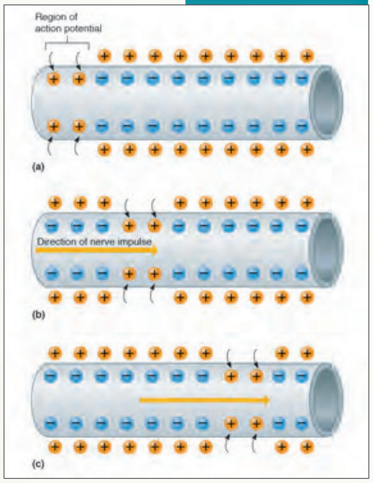

Myofibrils
Cisternae of sarcoplasmic reticulum
Transverse tubule
Nucleus
Sarcoplasmic reticulum
Openings into transverse tubules
Mitochondria
Thick and thin filaments
Sarcoplasm
Nucleus
Sarcolemma

This longitudinal section shows the interior structures of a muscle fiber revealing more detail of the myofibrils, and thick and thin filaments.

12th Edition


Region of action potential
(a)
Direction of conduction
(b)
(c)

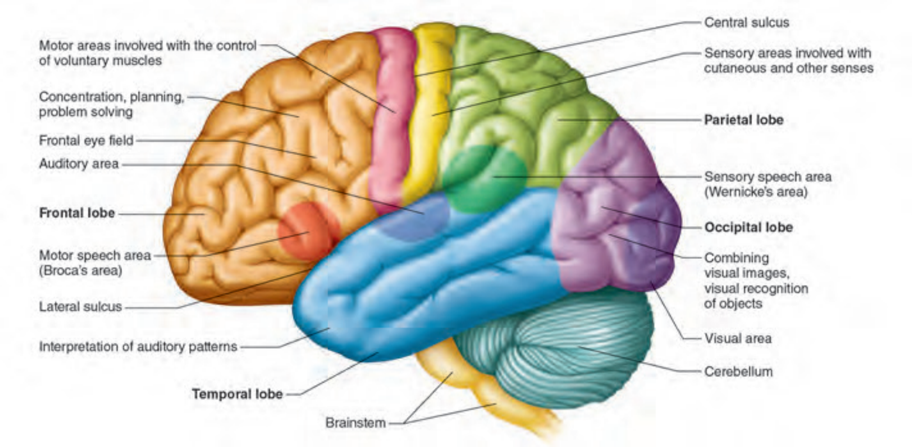
11th Edition


Region of action potential
(a)
Direction of nerve impulse
(b)
(c)

Color follows the movement of the action potential.

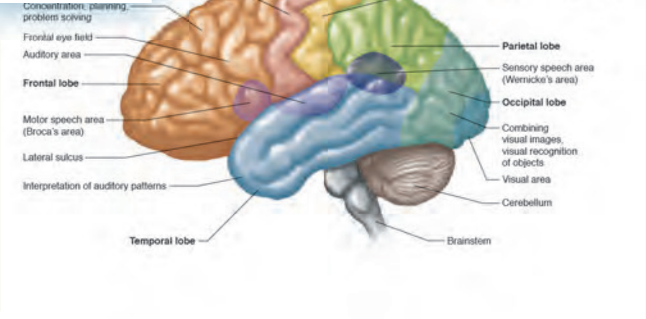
# DYNAMIC NEW ART PROGRAM

12th Edition

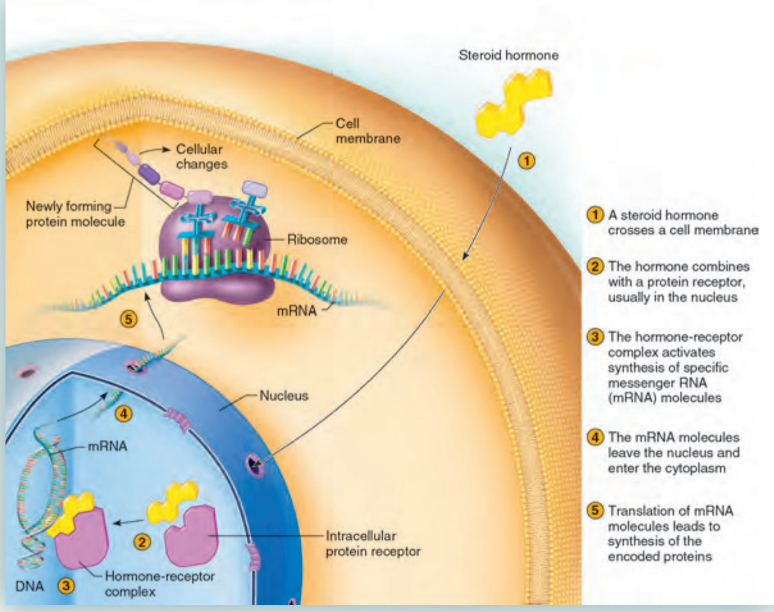

Motor areas involved with the control of voluntary muscles
Concentration, planning, problem solving
Frontal eye field
Auditory area
**Frontal lobe**
Motor speech area (Broca's area)
Lateral sulcus
Interpretation of auditory patterns
**Temporal lobe**
Brainstem
Central sulcus
Sensory areas involved with cutaneous and other senses
**Parietal lobe**
Sensory speech area (Wernicke's area)
**Occipital lobe**
Combining visual images, visual recognition of objects
Visual area
Cerebellum

Colors distinguish functional areas more readily and figures are more accurately drawn.

11th Edition


control
Concentration, planning, problem solving
Frontal eye field
Auditory area
**Frontal lobe**
Motor speech area (Broca's area)
Lateral sulcus
Interpretation of auditory patterns
**Temporal lobe**
Central sulcus
Sensory areas involved with cutaneous and other senses
**Parietal lobe**
Sensory speech area (Wernicke's area)
**Occipital lobe**
Combining visual images, visual recognition of objects
Visual area
Cerebellum
Brainstem

12th Edition


Steroid hormone
①
Cell membrane
Cellular changes
Newly forming protein molecule
Ribosome
mRNA
⑤
Nucleus
④
mRNA
②
DNA
③
Hormone-receptor complex
Intracellular protein receptor

① A steroid hormone crosses a cell membrane

② The hormone combines with a protein receptor, usually in the nucleus

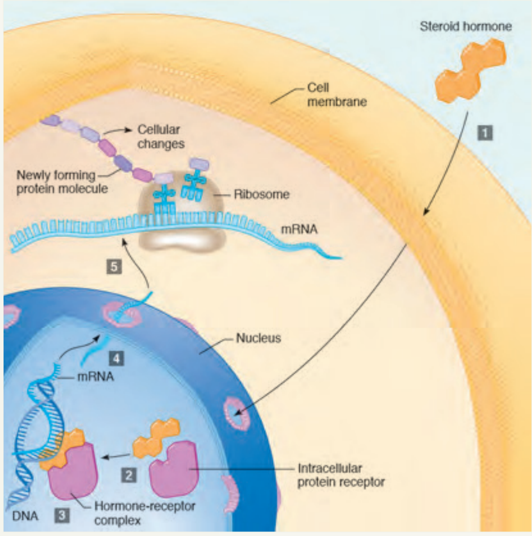
③ The hormone-receptor complex activates synthesis of specific messenger RNA (mRNA) molecules

④ The mRNA molecules leave the nucleus and enter the cytoplasm

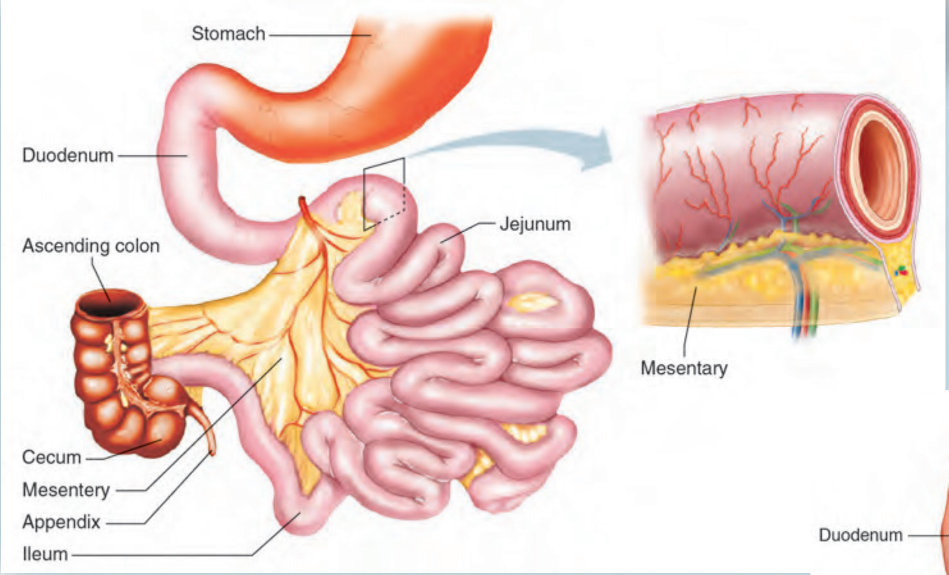
⑤ Translation of mRNA molecules leads to synthesis of the encoded proteins

The explanation has been moved out of the legend to become part of the figure.

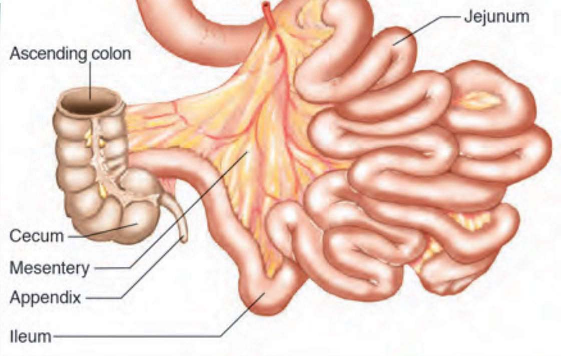
11th Edition


Steroid hormone
1
Cell membrane
Cellular changes
Newly forming protein molecule
Ribosome
mRNA
5
Nucleus
4
mRNA
2
DNA
3
Hormone-receptor complex
Intracellular protein receptor

**12th Edition**

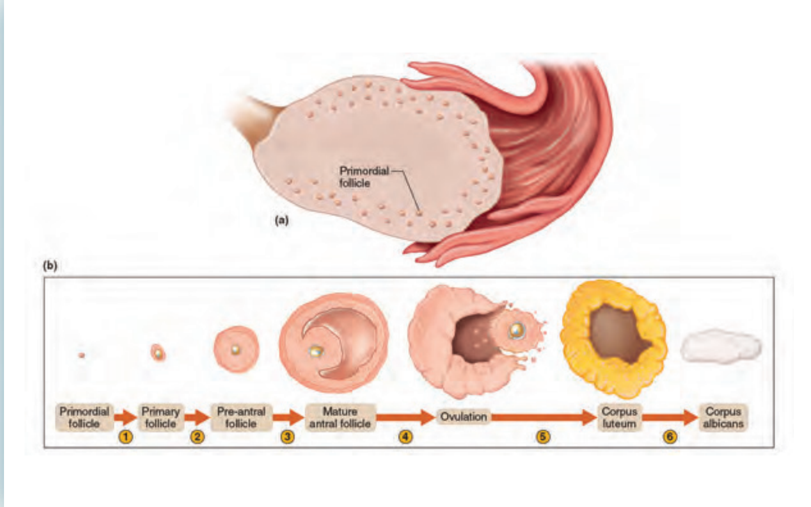

Stomach
Duodenum
Ascending colon
Jejunum
Mesentary
Cecum
Mesentery
Appendix
Ileum

**11th Edition**

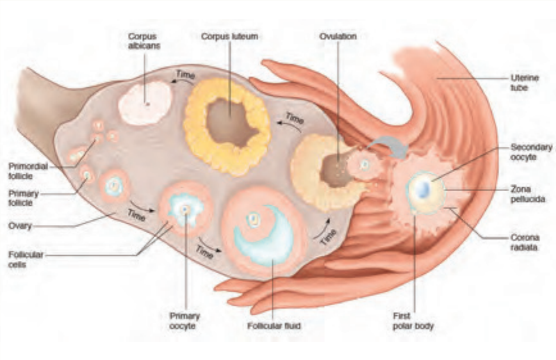

Stomach
Duodenum
Jejunum
Ascending colon
Cecum
Mesentery
Appendix
Ileum

New enlargement shows the detail in the structure of the mesentery.

**12th Edition**


Primordial follicle
(a)
(b)
Primordial follicle
①
Primary follicle
②
Pre-antral follicle
③
Mature antral follicle
④
Ovulation
⑤
Corpus luteum
⑥
Corpus albicans

**11th Edition**

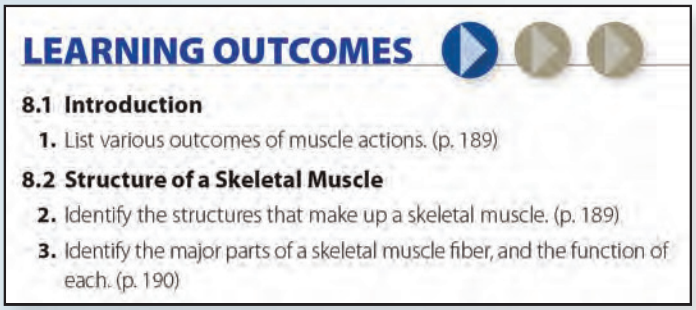

Corpus albicans
Corpus luteum
Ovulation
Time
Uterine tube
Secondary oocyte
Zona pellucida
Corona radiata
Primordial follicle
Primary follicle
Ovary
Follicular cells
Primary oocyte
Follicular fluid
First polar body

Process portrayed more accurately.

# Learn, Practice, Assess!

## Learn

**Learning Outcomes** open chapters, and are closely linked to Chapter Assessments and Integrative Assessments/Critical Thinking questions found at the end of each chapter.



LEARNING OUTCOMES

**8.1 Introduction**

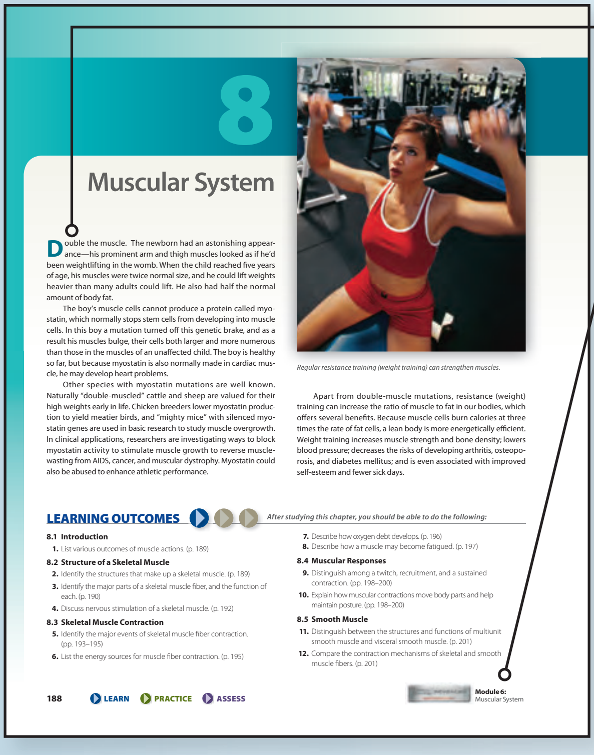
1. List various outcomes of muscle actions. (p. 189)

**8.2 Structure of a Skeletal Muscle**

2. Identify the structures that make up a skeletal muscle. (p. 189)
3. Identify the major parts of a skeletal muscle fiber, and the function of each. (p. 190)

### Learning tools to help you succeed. . .

Check out the Chapter Preview, *Foundations for Success*, on page 1. The Chapter Preview was specifically designed to help you **LEARN** how to study. It provides helpful study tips.



8

Muscular System

Double the muscle. The newborn had an astonishing appearance—his prominent arm and thigh muscles looked as if he'd been weightlifting in the womb. When the child reached five years of age, his muscles were twice normal size, and he could lift weights heavier than many adults could lift. He also had half the normal amount of body fat.

The boy's muscle cells cannot produce a protein called myostatin, which normally stops stem cells from developing into muscle cells. In this boy a mutation turned off this genetic brake, and as a result his muscles bulge, their cells both larger and more numerous than those in the muscles of an unaffected child. The boy is healthy so far, but because myostatin is also normally made in cardiac muscle, he may develop heart problems.

Other species with myostatin mutations are well known. Naturally "double-muscled" cattle and sheep are valued for their high weights early in life. Chicken breeders lower myostatin production to yield meatier birds, and "mighty mice" with silenced myostatin genes are used in basic research to study muscle overgrowth. In clinical applications, researchers are investigating ways to block myostatin activity to stimulate muscle growth to reverse muscle-wasting from AIDS, cancer, and muscular dystrophy. Myostatin could also be abused to enhance athletic performance.

*Regular resistance training (weight training) can strengthen muscles.*

Apart from double-muscle mutations, resistance (weight) training can increase the ratio of muscle to fat in our bodies, which offers several benefits. Because muscle cells burn calories at three times the rate of fat cells, a lean body is more energetically efficient. Weight training increases muscle strength and bone density; lowers blood pressure; decreases the risks of developing arthritis, osteoporosis, and diabetes mellitus; and is even associated with improved self-esteem and fewer sick days.

LEARNING OUTCOMES *After studying this chapter, you should be able to do the following:*

**8.1 Introduction**

1. List various outcomes of muscle actions. (p. 189)

**8.2 Structure of a Skeletal Muscle**

2. Identify the structures that make up a skeletal muscle. (p. 189)
3. Identify the major parts of a skeletal muscle fiber, and the function of each. (p. 190)
4. Discuss nervous stimulation of a skeletal muscle. (p. 192)

**8.3 Skeletal Muscle Contraction**

5. Identify the major events of skeletal muscle fiber contraction. (pp. 193–195)
6. List the energy sources for muscle fiber contraction. (p. 195)
7. Describe how oxygen debt develops. (p. 196)
8. Describe how a muscle may become fatigued. (p. 197)

**8.4 Muscular Responses**

9. Distinguish among a twitch, recruitment, and a sustained contraction. (pp. 198–200)
10. Explain how muscular contractions move body parts and help maintain posture. (pp. 198–200)

**8.5 Smooth Muscle**

11. Distinguish between the structures and functions of multiunit smooth muscle and visceral smooth muscle. (p. 201)
12. Compare the contraction mechanisms of skeletal and smooth muscle fibers. (p. 201)

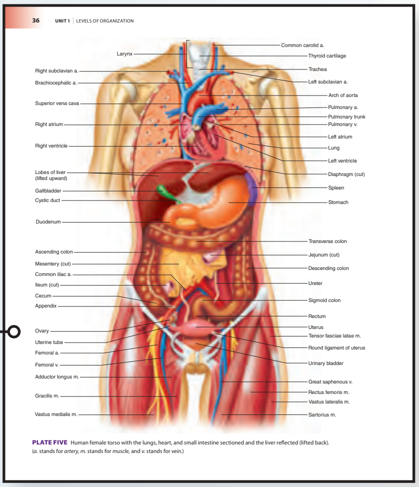
188 LEARN PRACTICE ASSESS

**Module 6:** Muscular System

- **Vignettes** lead into chapter content. They connect you to many areas of health care including technology, physiology, medical conditions, historical perspectives, and careers.
- **Anatomy and Physiology Revealed (APR) icon** at the beginning of each chapter tells you which system in APR applies to this chapter.

**Aids to Understanding Words** examines root words, stems, prefixes, suffixes, and pronunciations to help you build a solid anatomy and physiology vocabulary.

**Reference Plates** offer vibrant detail of body structures.



36 UNIT 1 | LEVELS OF ORGANIZATION

Common carotid a.
Larynx
Thyroid cartilage
Trachea
Right subclavian a.
Left subclavian a.
Brachiocephalic a.
Arch of aorta
Superior vena cava
Pulmonary a.
Pulmonary trunk
Right atrium
Pulmonary v.
Left atrium
Right ventricle
Lung
Left ventricle
Lobes of liver (lifted upward)
Diaphragm (cut)
Gallbladder
Spleen
Cystic duct
Stomach
Duodenum
Transverse colon
Ascending colon
Jejunum (cut)
Mesentery (cut)
Descending colon
Common iliac a.
Ureter
Ileum (cut)
Cecum
Sigmoid colon
Appendix
Rectum
Uterus
Ovary
Tensor fasciae latae m.
Uterine tube
Round ligament of uterus
Femoral a.
Urinary bladder
Femoral v.
Adductor longus m.
Great saphenous v.
Rectus femoris m.
Gracilis m.
Vastus lateralis m.
Vastus medialis m.
Sartorius m.

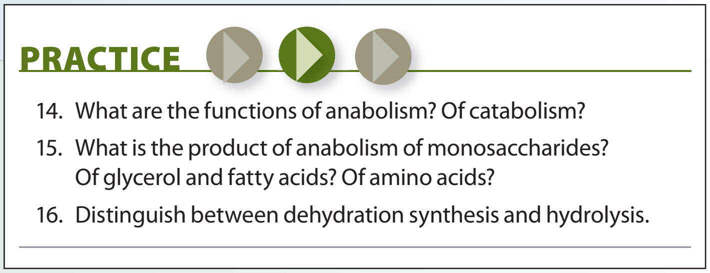
**PLATE FIVE** Human female torso with the lungs, heart, and small intestine sectioned and the liver reflected (lifted back). (*a.* stands for *artery*, *m.* stands for *muscle*, and *v.* stands for *vein*.)

## Practice

Practice with a question or series of questions after major sections. They will test your understanding of the material.

### Interesting applications help you practice and apply knowledge. . .

**Figure Questions** allow an additional assessment. Found on key figures throughout the chapter.



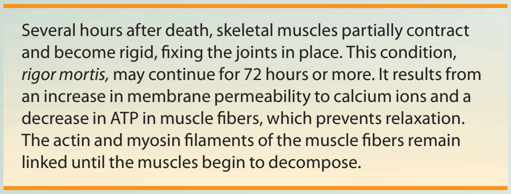
PRACTICE

14. What are the functions of anabolism? Of catabolism?
15. What is the product of anabolism of monosaccharides? Of glycerol and fatty acids? Of amino acids?
16. Distinguish between dehydration synthesis and hydrolysis.

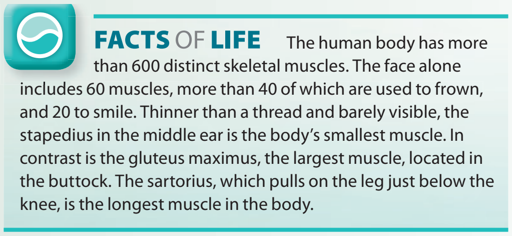
**FIGURE 8.5** APR A neuromuscular junction includes the end of a motor neuron and the motor end plate of a muscle fiber.

Q *How does neurotransmitter released into the synaptic cleft reach the muscle fiber membrane?*
**Answer can be found in Appendix F on page 582.**

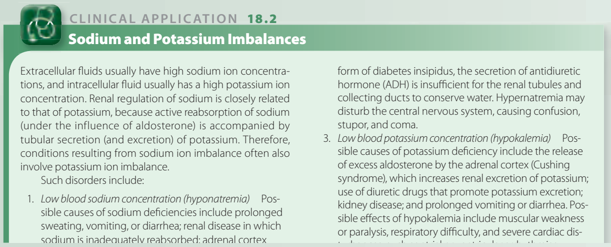
**Boxed information** expands on the concepts discussed in the text.


Several hours after death, skeletal muscles partially contract and become rigid, fixing the joints in place. This condition, *rigor mortis,* may continue for 72 hours or more. It results from an increase in membrane permeability to calcium ions and a decrease in ATP in muscle fibers, which prevents relaxation. The actin and myosin filaments of the muscle fibers remain linked until the muscles begin to decompose.

**Facts of Life** provides interesting bits of anatomy and physiology information, adding a touch of wonder to chapter topics.


**FACTS OF LIFE** The human body has more than 600 distinct skeletal muscles. The face alone includes 60 muscles, more than 40 of which are used to frown, and 20 to smile. Thinner than a thread and barely visible, the stapedius in the middle ear is the body's smallest muscle. In contrast is the gluteus maximus, the largest muscle, located in the buttock. The sartorius, which pulls on the leg just below the knee, is the longest muscle in the body.

**Clinical Applications** present disorders, physiological responses to environmental factors, and other topics of general interest and applies them to clinical situations.


CLINICAL APPLICATION 18.2

**Sodium and Potassium Imbalances**

Extracellular fluids usually have high sodium ion concentrations, and intracellular fluid usually has a high potassium ion concentration. Renal regulation of sodium is closely related to that of potassium, because active reabsorption of sodium (under the influence of aldosterone) is accompanied by tubular secretion (and excretion) of potassium. Therefore, conditions resulting from sodium ion imbalance often also involve potassium ion imbalance.

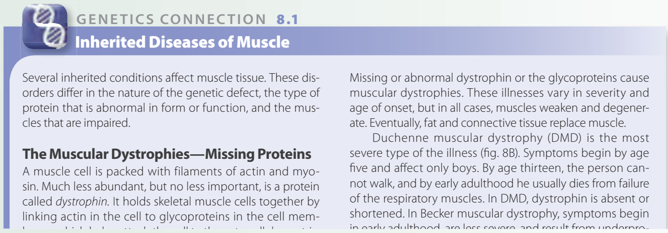
Such disorders include:

1. *Low blood sodium concentration (hyponatremia)* Possible causes of sodium deficiencies include prolonged sweating, vomiting, or diarrhea; renal disease in which sodium is inadequately reabsorbed; adrenal cortex

form of diabetes insipidus, the secretion of antidiuretic hormone (ADH) is insufficient for the renal tubules and collecting ducts to conserve water. Hypernatremia may disturb the central nervous system, causing confusion, stupor, and coma.

3. *Low blood potassium concentration (hypokalemia)* Possible causes of potassium deficiency include the release of excess aldosterone by the adrenal cortex (Cushing syndrome), which increases renal excretion of potassium; use of diuretic drugs that promote potassium excretion; kidney disease; and prolonged vomiting or diarrhea. Possible effects of hypokalemia include muscular weakness or paralysis, respiratory difficulty, and severe cardiac dis-

**Genetics Connections** explore the molecular underpinnings of familiar as well as not so familiar illnesses. Read about such topics as ion channel disorders, muscular dystrophy, and cystic fibrosis.


GENETICS CONNECTION 8.1

**Inherited Diseases of Muscle**

Several inherited conditions affect muscle tissue. These disorders differ in the nature of the genetic defect, the type of protein that is abnormal in form or function, and the muscles that are impaired.

**The Muscular Dystrophies—Missing Proteins**

A muscle cell is packed with filaments of actin and myosin. Much less abundant, but no less important, is a protein called *dystrophin*. It holds skeletal muscle cells together by linking actin in the cell to glycoproteins in the cell mem-

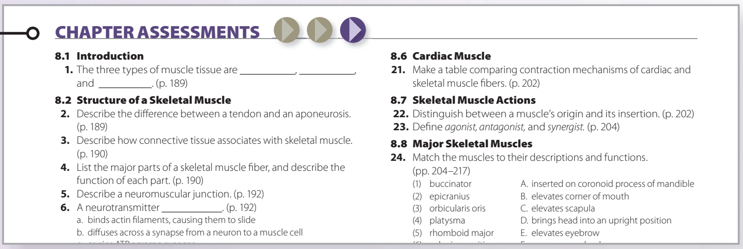
Missing or abnormal dystrophin or the glycoproteins cause muscular dystrophies. These illnesses vary in severity and age of onset, but in all cases, muscles weaken and degenerate. Eventually, fat and connective tissue replace muscle.

Duchenne muscular dystrophy (DMD) is the most severe type of the illness (fig. 8B). Symptoms begin by age five and affect only boys. By age thirteen, the person cannot walk, and by early adulthood he usually dies from failure of the respiratory muscles. In DMD, dystrophin is absent or shortened. In Becker muscular dystrophy, symptoms begin

# Assess

## Tools to help you make the connection and master anatomy & physiology!

**Chapter Assessments** check your understanding of the chapter's learning outcomes.


**CHAPTER ASSESSMENTS**

**8.1 Introduction**

**1.** The three types of muscle tissue are ___________, ___________, and ___________. (p. 189)

**8.2 Structure of a Skeletal Muscle**

**2.** Describe the difference between a tendon and an aponeurosis. (p. 189)

**3.** Describe how connective tissue associates with skeletal muscle. (p. 190)

**4.** List the major parts of a skeletal muscle fiber, and describe the function of each part. (p. 190)

**5.** Describe a neuromuscular junction. (p. 192)

**6.** A neurotransmitter _____________. (p. 192)
  a. binds actin filaments, causing them to slide
  b. diffuses across a synapse from a neuron to a muscle cell

**8.6 Cardiac Muscle**

**21.** Make a table comparing contraction mechanisms of cardiac and skeletal muscle fibers. (p. 202)

**8.7 Skeletal Muscle Actions**

**22.** Distinguish between a muscle's origin and its insertion. (p. 202)

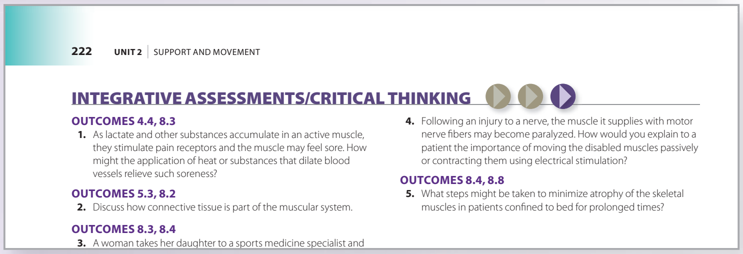
**23.** Define *agonist, antagonist,* and *synergist.* (p. 204)

**8.8 Major Skeletal Muscles**

**24.** Match the muscles to their descriptions and functions. (pp. 204–217)

| | |
|---|---|
| (1) buccinator | A. inserted on coronoid process of mandible |
| (2) epicranius | B. elevates corner of mouth |
| (3) orbicularis oris | C. elevates scapula |
| (4) platysma | D. brings head into an upright position |
| (5) rhomboid major | E. elevates eyebrow |

**Integrative Assessments/Critical Thinking questions** allow you to connect and apply information from previous chapters as well as information within the current chapter.


222 UNIT 2 | SUPPORT AND MOVEMENT

**INTEGRATIVE ASSESSMENTS/CRITICAL THINKING**

**OUTCOMES 4.4, 8.3**

**1.** As lactate and other substances accumulate in an active muscle, they stimulate pain receptors and the muscle may feel sore. How might the application of heat or substances that dilate blood vessels relieve such soreness?

**OUTCOMES 5.3, 8.2**

**2.** Discuss how connective tissue is part of the muscular system.

**OUTCOMES 8.3, 8.4**

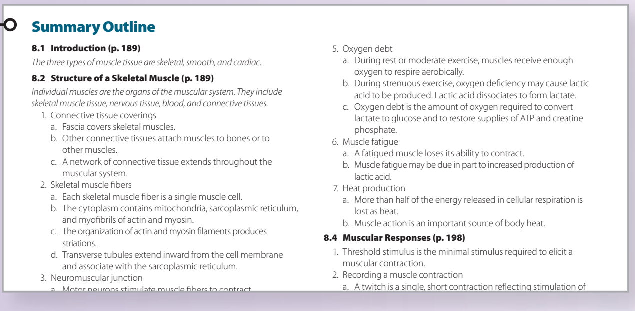
**3.** A woman takes her daughter to a sports medicine specialist and

**4.** Following an injury to a nerve, the muscle it supplies with motor nerve fibers may become paralyzed. How would you explain to a patient the importance of moving the disabled muscles passively or contracting them using electrical stimulation?

**OUTCOMES 8.4, 8.8**

**5.** What steps might be taken to minimize atrophy of the skeletal muscles in patients confined to bed for prolonged times?

**Chapter Summary Outlines** help you review the chapter's main ideas.


**Summary Outline**

**8.1 Introduction (p. 189)**

*The three types of muscle tissue are skeletal, smooth, and cardiac.*

**8.2 Structure of a Skeletal Muscle (p. 189)**

*Individual muscles are the organs of the muscular system. They include skeletal muscle tissue, nervous tissue, blood, and connective tissues.*

1. Connective tissue coverings
   a. Fascia covers skeletal muscles.
   b. Other connective tissues attach muscles to bones or to other muscles.
   c. A network of connective tissue extends throughout the muscular system.
2. Skeletal muscle fibers
   a. Each skeletal muscle fiber is a single muscle cell.
   b. The cytoplasm contains mitochondria, sarcoplasmic reticulum, and myofibrils of actin and myosin.
   c. The organization of actin and myosin filaments produces striations.
   d. Transverse tubules extend inward from the cell membrane and associate with the sarcoplasmic reticulum.
3. Neuromuscular junction
   a. Motor neurons stimulate muscle fibers to contract.

5. Oxygen debt
   a. During rest or moderate exercise, muscles receive enough oxygen to respire aerobically.
   b. During strenuous exercise, oxygen deficiency may cause lactic acid to be produced. Lactic acid dissociates to form lactate.
   c. Oxygen debt is the amount of oxygen required to convert lactate to glucose and to restore supplies of ATP and creatine phosphate.
6. Muscle fatigue
   a. A fatigued muscle loses its ability to contract.
   b. Muscle fatigue may be due in part to increased production of lactic acid.
7. Heat production
   a. More than half of the energy released in cellular respiration is lost as heat.
   b. Muscle action is an important source of body heat.

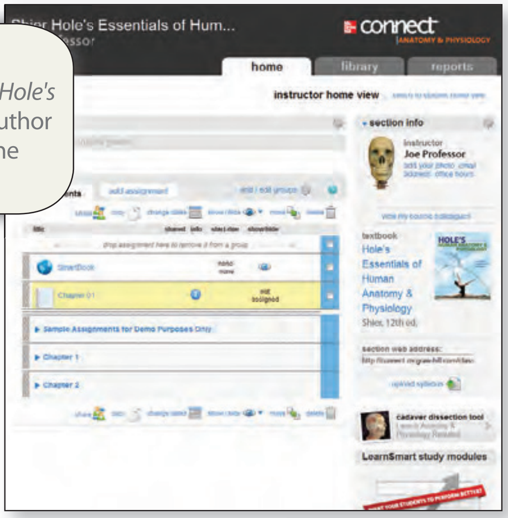
**8.4 Muscular Responses (p. 198)**

1. Threshold stimulus is the minimal stimulus required to elicit a muscular contraction.
2. Recording a muscle contraction
   a. A twitch is a single, short contraction reflecting stimulation of

# connect® plus+

## ANATOMY & PHYSIOLOGY

Hi! I'm Leslie Day. We know that it's frustrating when your online homework questions contradict your textbook. In this edition of *Hole's Essentials of Human Anatomy & Physiology*, Julie and I joined the author team to ensure that our online resources correlate directly with the information and learning tools you will find in the textbook.


Shier Hole's Essentials of Hum...
connect ANATOMY & PHYSIOLOGY
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Joe Professor
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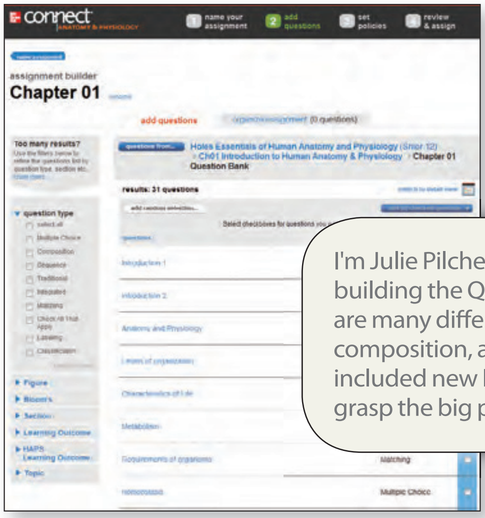
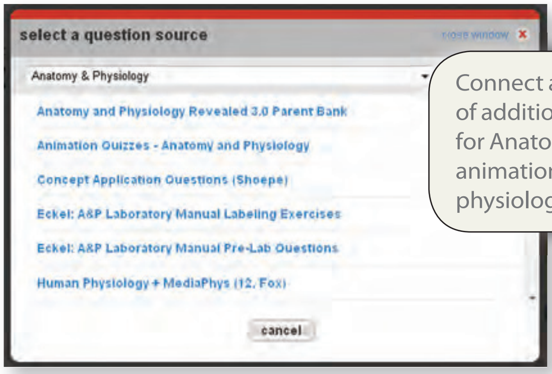

connect ANATOMY & PHYSIOLOGY
name your assignment
add questions
set policies
review & assign
assignment builder
Chapter 01
add questions
Too many results?
question type
Figure
Bloom's
Section
Learning Outcome
HAPS Learning Outcome
Topic
Holes Essentials of Human Anatomy and Physiology (Shier 12)
Ch01 Introduction to Human Anatomy & Physiology
Chapter 01
Question Bank
results: 31 questions
Matching
Multiple Choice

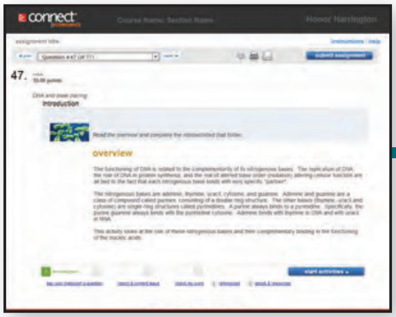
I'm Julie Pilcher. You can call us the Digital Authors! We work on building the Question Bank in Connect. We make sure that there are many different question types, like labeling, multiple choice, composition, and sequencing. For the twelfth edition we have included new Integrated questions. These questions help the student grasp the big picture by connecting concepts throughout the course.

We also ensure that there is an appropriate number of questions for each learning outcome in the chapter. We tagged the questions not only to learning outcomes in the text but also to the Human Anatomy & Physiology Society (HAPS) Learning Outcomes. This makes it easy for the instructor to find just the question they want. We also make sure that there is a variety of questions with different Bloom's Taxonomy levels!

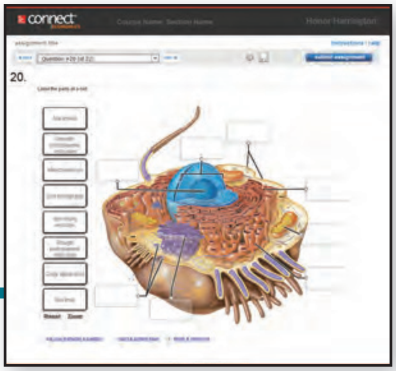

select a question source
close window ×
Anatomy & Physiology
Anatomy and Physiology Revealed 3.0 Parent Bank
Animation Quizzes - Anatomy and Physiology
Concept Application Questions (Shoepe)
Eckel: A&P Laboratory Manual Labeling Exercises
Eckel: A&P Laboratory Manual Pre-Lab Questions
Human Physiology + MediaPhys (12, Fox)
cancel

Connect also gives the instructor access to a lot of additional material. They can access questions for Anatomy & Physiology Revealed, a variety of animations, and also every other anatomy and physiology title from McGraw-Hill Education.

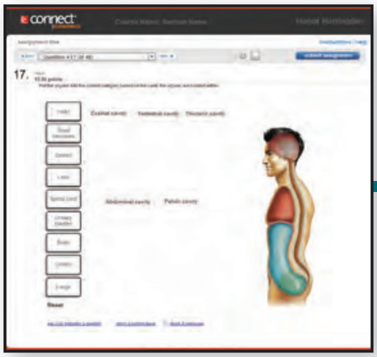
Here are some of the question types we have created for the twelfth edition!



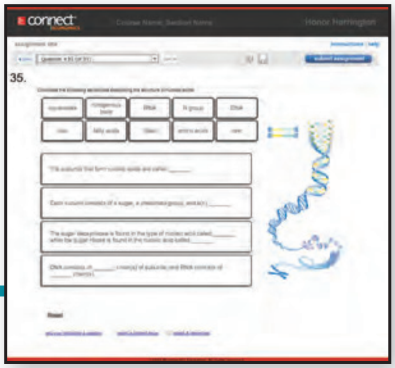
**Integrated activities** use a series of interactive questions to allow students to apply their new knowledge and/or see how different processes are related. Some integrated questions also include animations to help the visual learner.



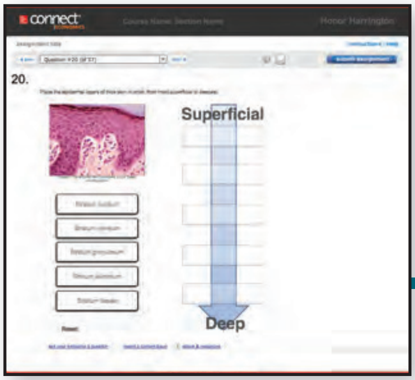
**Labeling activities** allow students to identify structures using figures from the text. Also available are questions in which functions or descriptions are used as drag-and-drop labels.



**Classification questions** ask students to place terms into appropriate categories, to recognize the differences and similarities in structures.



**Composition questions** allow for completion of a series of sentences describing structures, processes, or functions. Some composition questions then require arranging the completed sentences in a logical order.



**Sequence questions** have been designed around ordering physiological processes or some anatomical topics, such as listing structures' locations from proximal to distal.

# TEACHING AND LEARNING SUPPLEMENTS

## Text Website – www.mhhe.com/shieress12

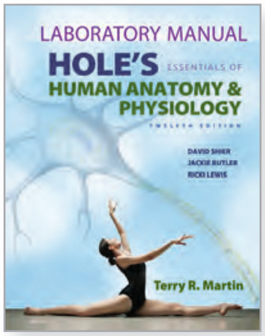
Ancillary Correlation Guide—instructors will find this guide invaluable. McGraw-Hill offers a variety of ancillary products to accompany our texts. The authors have gone through the ancillaries and correlated them to the specific Learning Outcomes found at the beginning of each chapter! The ancillaries that are correlated to the specific Learning Outcomes for *Hole's Essentials of Human Anatomy & Physiology*, Twelfth Edition:

- Ph.I.L.S. 4.0
- MediaPhys 3.0
- Anatomy & Physiology Revealed
- Virtual Anatomy Dissection Review
- Student Study Guide—offers chapter overviews, chapter outcomes, focus questions, mastery tests, study activities, and mastery test answers.

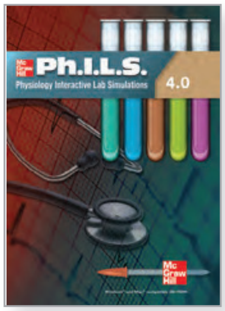
## McGraw-Hill's Presentation Tools

Presentation Materials for Lecture and Lab—incorporate customized lectures, visually enhanced test and quizzes, compelling course websites, or attractive printed support materials.

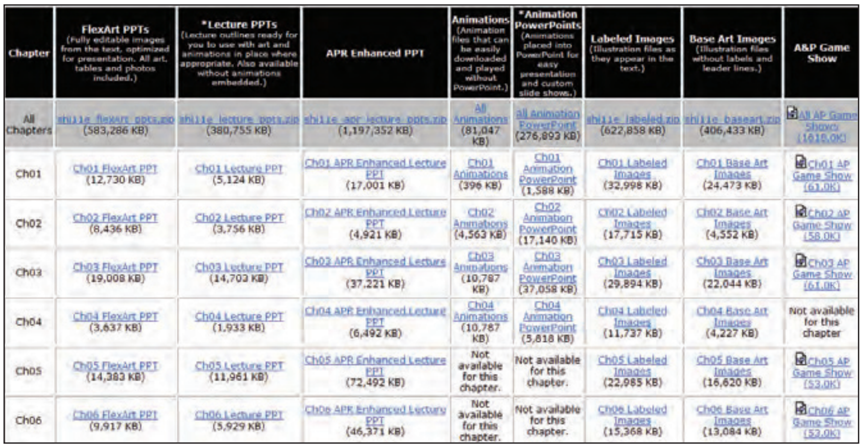
- A complete set of pre-made PowerPoints linking **Anatomy & Physiology Revealed** to text material is available for your use!
- A complete set of animation-embedded PowerPoint slides is available.
- Along with our online digital library containing photos, artwork, and animations, we also offer **FlexArt**. FlexArt allows the instructor to customize artwork.
- Computerized test bank edited by the **Author Team** is powered by McGraw-Hill's flexible electronic testing program EZ Test Online.



***Laboratory Manual for Hole's Essentials of Human Anatomy & Physiology, Twelfth Edition,*** by Terry R. Martin, Kishwaukee College, is designed to accompany the twelfth edition of *Hole's Essentials of Human Anatomy & Physiology*.



**NEW! Ph.I.L.S. 4.0** has been updated! Users have requested and we are providing five new exercises (Respiratory Quotient, Weight & Contraction, Insulin and Glucose Tolerance, Blood Typing, and Anti-Diuretic Hormone). Ph.I.L.S. 4.0 is the perfect way to reinforce key physiology concepts with powerful lab experiments. Created by Dr. Phil Stephens at Villanova University, this program offers 42 laboratory simulations that may be used to supplement or substitute for wet labs. All 42 labs are self-contained experiments—no lengthy instruction manual required. Users can adjust variables, view outcomes, make predictions, draw conclusions, and print lab reports. This easy-to-use software offers the flexibility to change the parameters of the lab experiment. There is no limit!



| Chapter | FlexArt PPTs (Fully editable images from the text, optimized for presentation. All art, tables and photos included.) | *Lecture PPTs (Lecture outlines ready for you to use with art and animations in place where appropriate. Also available without animations embedded.) | APR Enhanced PPT | Animations (Animation files that can be easily downloaded and played without PowerPoint.) | *Animation PowerPoints (Animations placed into PowerPoint for easy presentation and custom slide shows.) | Labeled Images (Illustration files as they appear in the text.) | Base Art Images (Illustration files without labels and leader lines.) | A&P Game Show |
|---|---|---|---|---|---|---|---|---|
| All Chapters | shi11e_flexart_ppts.zip (583,286 KB) | shi11e_lecture_ppts.zip (380,755 KB) | shi11e_apr_lecture_ppts.zip (1,197,352 KB) | All Animations (81,047 KB) | All Animation PowerPoint (276,893 KB) | shi11e_labeled.zip (622,858 KB) | shi11e_baseart.zip (406,433 KB) | All AP Game Shows (1610.0K) |
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| Ch04 | Ch04 FlexArt PPT (3,637 KB) | Ch04 Lecture PPT (1,933 KB) | Ch04 APR Enhanced Lecture PPT (6,492 KB) | Ch04 Animations (10,787 KB) | Ch04 Animation PowerPoint (5,818 KB) | Ch04 Labeled Images (11,737 KB) | Ch04 Base Art Images (4,227 KB) | Not available for this chapter |
| Ch05 | Ch05 FlexArt PPT (14,383 KB) | Ch05 Lecture PPT (11,961 KB) | Ch05 APR Enhanced Lecture PPT (72,492 KB) | Not available for this chapter. | Not available for this chapter. | Ch05 Labeled Images (22,985 KB) | Ch05 Base Art Images (16,620 KB) | Ch05 AP Game Show (53.0K) |
| Ch06 | Ch06 FlexArt PPT (9,917 KB) | Ch06 Lecture PPT (5,929 KB) | Ch06 APR Enhanced Lecture PPT (46,371 KB) | Not available for this chapter. | Not available for this chapter. | Ch06 Labeled Images (15,368 KB) | Ch06 Base Art Images (13,084 KB) | Ch06 AP Game Show (53.0K) |

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Any textbook is the result of hard work by a large team. Although we directed the revision, many "behind-the-scenes" people at McGraw-Hill were indispensable to the project. We would like to thank our editorial team of Jim Connely, Marija Magner, and Fran Simon; Rosie Ellis, marketing manager; our production team, which included Jayne Klein, Sandy Ludovissy, Tara McDermott, John Leland, and Laura Bies. We would also like to thank copyeditor Wendy Nelson, freelance photo researcher Toni Michaels , and Imagineering project manager Alicia Elliott; and most of all, John Hole, for giving us the opportunity and freedom to continue his classic work. We also thank our wonderfully patient families for their support.

David Shier
Jackie Butler
Ricki Lewis

## A NOTE FROM THE AUTHORS

### To the Student

Welcome! As you read this (with your eyes) and understand it (with your brain), perhaps turning to the next page (with muscle actions of your fingers, hand, forearm, and arm), you are using the human body to do so. Indeed, some of you may be using your fingers, hand, forearm, and arm to read through the eBook on your computer, tablet, or smartphone. Whether you use traditional or new technology, the twelfth edition of *Hole's Essentials of Human Anatomy & Physiology* offers an interesting and readable introduction to how the human body accomplishes these tasks. The functioning of the body is not simple, and at times understanding may not seem easy, but learning how the body works is always fascinating and can be both useful and fun!

Many of you are on a path toward a career in health care, athletics, science, or education. Be sure to check out the new Career Corners in every chapter. They present interesting options for future careers. Balancing family, work, and academics is challenging, but try to look at this course not as a hurdle along your way but as a stepping stone. We have written this book to help you succeed in your coursework and to help prepare you to make that journey to a successful and rewarding career.

### To the Teacher

With this edition of *Hole's Essentials of Human Anatomy & Physiology*, we welcome two new authors. Leslie Day and Julie Pilcher are further developing LearnSmart and Connect and fully integrating them with the traditional elements of Hole's. We are extremely excited that Hole's is keeping pace with the ever-changing array of technologies available to support teaching and learning.

The Learn, Practice, Assess approach continues with this twelfth edition. Each chapter opens with Learning Outcomes, contains many opportunities to Practice throughout, and closes with Assessments that are closely tied to the Learning Outcomes. Students can use this feature not only to focus their study efforts, but also to take an active role in monitoring their own progress toward mastering the material. All of these resources are described in more detail in the Chapter Preview/Foundations for Success beginning on page 1.

David Shier, Jackie Butler, Ricki Lewis, Leslie Day, and Julie Pilcher

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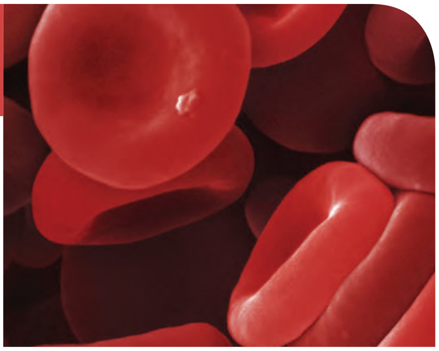

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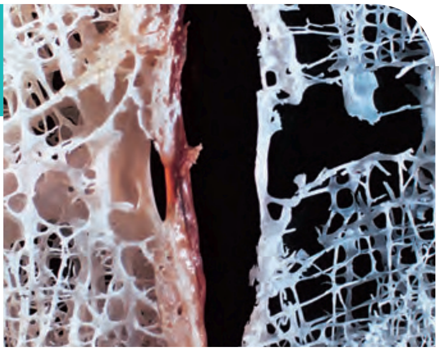

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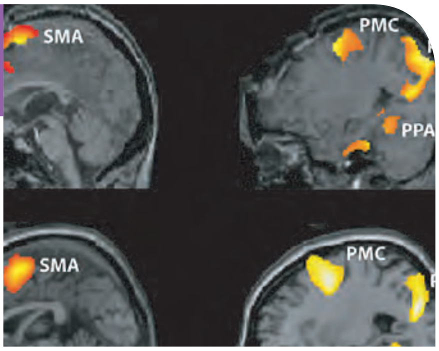

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# CHAPTER PREVIEW

## Foundations for Success

The Chapter Preview not only provides great study tips to offer a foundation for success, but it also offers tips on how to utilize this particular text.

*A photo on the opening page for each chapter generates interest.*

An opening vignette discusses current events or research news relating to the subject matter in the chapter. These vignettes apply the concepts learned in the study of anatomy and physiology.

Pay attention. It is a beautiful day. You can't help but stare wistfully out the window, the scent of spring blooms and sound of birds making it impossible to concentrate on what the instructor is saying. Gradually, the lecture fades as you become aware of your own breathing, the beating of your heart, and the sweat that breaks out on your forehead in response to the radiant heat from the glorious day. Suddenly your reverie is cut short—a classmate has dropped a human anatomy and physiology textbook on the floor. You jump. Your heart hammers and a flash of fear grips your chest, but you soon realize what has happened and recover.

The message is clear: pay attention. So you do, tuning out the great outdoors and focusing on the class. In this course, you will learn all about the events that you have just experienced, including your response to the sudden stimulation. This is a good reason to stay focused.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

**P.1 Introduction**

1. Explain the importance of an individualized approach to learning. (p. 2)

**P.2 Strategies for Your Success**

2. Summarize what you should do before attending class. (pp. 2–3)
3. Identify student activities that enhance classroom experience. (p. 6)
4. List and describe several study techniques that can facilitate learning new material. (p. 7)

Each chapter has a list of learning outcomes indicating the knowledge you should gain as you work through the chapter. (Note the blue learn arrow following the title of this section.) These outcomes are intended to help you master the similar outcomes set by your instructor. The outcomes are tied directly to assessments of knowledge gained.

This digital tool, as indicated here and with the APR icons within the chapters, allows you to explore the human body in depth through cadaver dissection and histology preparations. It also offers animations on chapter concepts.

Anatomy & Physiology REVEALED®
aprevealed.com

This section introduces building blocks of words that your instructor may assign. Learning them is a good investment of your time, because they can be used over and over and apply to many of the terms you will use in your career. Appendix A (p. 577) has a comprehensive list of these prefixes, suffixes, and root words.

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**ana-** [up] *ana*tomy: the study of breaking up the body into its parts.

**multi-** [many] *multi*tasking: performing several tasks simultaneously.

**physio-** [relationship to nature] *physi*ology: the study of how body parts function.

---

## P.1 | Introduction

The first section of each chapter is an overview that tells you what to expect and why the subject matter is important.

Studying the human body can be overwhelming at times. The new terminology, used to describe body parts and how they work, can make it seem as if you are studying a foreign language. Learning all the parts of the body, along with the composition of each part, and how each part fits with the other parts to make the whole requires memorization. Understanding the way each body part works individually, as well as body parts working together, requires higher levels of knowledge, comprehension, and application. Identifying underlying structural similarities, from the macroscopic to the microscopic levels of body organization, taps more subtle critical thinking skills. This chapter will catalyze success in this active process of learning. (Remember that while the skills and tips discussed in this chapter relate to learning anatomy and physiology, they can be applied to other subjects.)

Learning occurs in different ways or modes. Most students use several modes (multimodal), but are more comfortable and use more effectively one or two, often referred to as learning styles. Some students prefer to read the written word to remember it and the concept it describes or to actually write the words; others learn best by looking at visual representations, such as photographs and drawings. Still others learn most effectively by hearing the information or explaining it to someone else. For some learners, true understanding remains elusive until a principle is revealed in a laboratory or clinical setting that provides a memorable context and engages all of the senses. This text accommodates the range of learning styles. Read-write learners will appreciate the lists, definitions (glossary), and tables. Visual learners will discover many diagrams, flow charts, and figures, all with consistent and purposeful use of color. For example, a particular bone is always the same color in the figures where bones are color coded. Auditory learners will find pronunciations for new scientific terms to help sound them out, and kinesthetic learners can relate real-life examples and applications to their own activities.

After each major section, a question or series of questions tests your understanding of the material and enables you to practice using the information. (Note the green practice arrow preceding the questions below.) If you cannot answer the question(s), you should reread that section, being on the lookout for the answer(s)

### PRACTICE

1. List some difficulties a student may experience when studying the human body.
2. Describe the ways that people learn.

---

## P.2 | Strategies for Your Success

Major divisions within a chapter are called "A-heads." They are numbered sequentially and entitled with very large, blue type to designate major content areas.

Many strategies for academic success are common sense, but it might help to review them. You may encounter new and helpful methods of learning.

The major divisions are subdivided into "B-heads," which are identified by large, black type. These will help you organize the concepts upon which the major divisions are built.

### Before Class

Before attending class, prepare by reading and outlining or taking notes on the assigned pages of the text. If outlining, leave adequate space between entries to allow room for note-taking during lectures. Or, fold each page of notes taken before class in half so that class notes can be written on the blank side of the paper across from the reading notes on the same topic. This strategy introduces the topics of the next class lecture discussion, as well as new terms. Some students team a vocabulary list with each chapter's notes. Take the notes from the reading to class and expand them. At a minimum, the student should at least skim the text, reading the A-heads and B-heads and the summary outline to become acquainted with the topics and vocabulary before class.

As you read, you may feel the need for a "study break" or to "chill out." Other times, you may just need to shift gears. Try the following. Throughout the book shaded boxes present sidelights to the main text. Indeed, some of these may cover topics that your instructor chooses to highlight. Read them! They are interesting, informative, and a change of pace.

**FACTS OF LIFE** The skeleton of an average 160-pound body weighs about 29 pounds.

CLINICAL APPLICATION **9.1**

### Factors Affecting Synaptic Transmission

Impulses reaching synaptic knobs too rapidly can exhaust neurotransmitter supplies, and impulse conduction ceases until more neurotransmitters are synthesized. This happens during an epileptic seizure. Abnormal and too rapid impulses originate from certain brain cells and reach skeletal muscle fibers, stimulating violent contractions. In time, the synaptic knobs run out of neurotransmitters and the seizure subsides.

A drug called Dilantin (diphenylhydantoin) treats seizure disorders by blocking gated sodium channels, thereby limiting the frequency at which action potentials can occur. Many other drugs affect synaptic transmission. For example, caffeine in coffee, tea, and cola drinks stimulates nervous system activity by lowering the thresholds at synapses so that neurons are more easily excited. Antidepressants called "selective serotonin reuptake inhibitors" (SSRIs) keep the neurotransmitter serotonin in synapses longer, compensating for a still little-understood deficit that presumably causes depression.

Health-care workers repeatedly monitor patients' *vital signs*—observable body functions that reflect essential metabolic activities. Vital signs indicate that a person is alive. Assessment of vital signs includes measuring body temperature and blood pressure and monitoring rates and types of pulse and breathing movements. Absence of vital signs signifies death. A person who has died displays no spontaneous muscular movements, including those of the breathing muscles and beating heart. A dead person does not respond to stimuli and has no reflexes, such as the knee-jerk reflex and the pupillary reflexes of the eye. Brain waves cease with death, as demonstrated by a flat electroencephalogram (EEG), which signifies a lack of metabolic activity in the brain.

Students using this book and taking various courses are often preparing for careers in health care. In some cases students may be undecided as to a specific area or specialty. The Career Corner presents a description of a particular career choice with each chapter. If it doesn't describe a career that you seek, perhaps it will give you a better sense of what some of your coworkers and colleagues do!

CAREER CORNER

### Massage Therapist

The middle-aged woman feels something give way in her left knee as she lands from a jump in her dance class. She limps away between her much younger classmates, in great pain. At home, she uses "RICE"—rest, ice, compression, elevation—then has a friend take her to an urgent care clinic, where a physician diagnoses patellar tendinitis, or "jumper's knee." Frequent jumping followed by lateral movements caused the injury.

Three days later, at her weekly appointment with a massage therapist for stress relief, the woman mentions the injury. Over the next few weeks, the massage therapist applies light pressure to the injured area to stimulate circulation, and applies friction in a transverse pattern to break up scar tissue and relax the muscles. She also massages the muscles to improve flexibility.

A massage therapist manipulates soft tissues, using combinations of pressing, stroking, kneading, compressing, and vibrating, to relieve pain and reduce stress. Training includes 300 to 1,000 hours of class time, hands-on practice, and continuing education. Specialties include pediatrics, sports injuries, and even applying massage techniques to racehorses.

## GENETICS CONNECTION 16.1

## Cystic Fibrosis

Young children who cannot pronounce the name of their disease call it "65 Roses." Cystic fibrosis (CF) is an inherited defect in ion channels that control chloride movement out of cells in certain organs. In the lungs, thick, sticky mucus accumulates and creates an environment hospitable to certain bacteria that are not common in healthy lungs. A mucus-clogged pancreas prevents digestive secretions from reaching the intestines, impairing nutrient digestion and absorption. A child with CF has trouble breathing and maintaining weight.

CF is inherited from two carrier parents, and affects about 30,000 people in the United States and about 70,000 worldwide. Many others may have milder cases, with recurrent respiratory infections. More than 1600 mutations have been recognized in the cystic fibrosis transmembrane receptor (*CFTR*) gene, which encodes the chloride channel protein. Today newborns with CF are diagnosed using a genetic test shortly after birth, but years ago the first signs were typically "failure to thrive," salty sweat, and foul-smelling stools.

When CF was recognized in 1938, life expectancy was only five years, but today median survival is about age forty, with many patients living longer, thanks to drug treatments. Inhaled antibiotics control the respiratory infections, and daily "bronchial drainage" exercises shake stifling mucus from the lungs. A vibrating vest worn for half-hour periods two to four times a day also loosens mucus. Digestive enzymes mixed into soft foods enhance nutrient absorption, although some patients require feeding tubes.

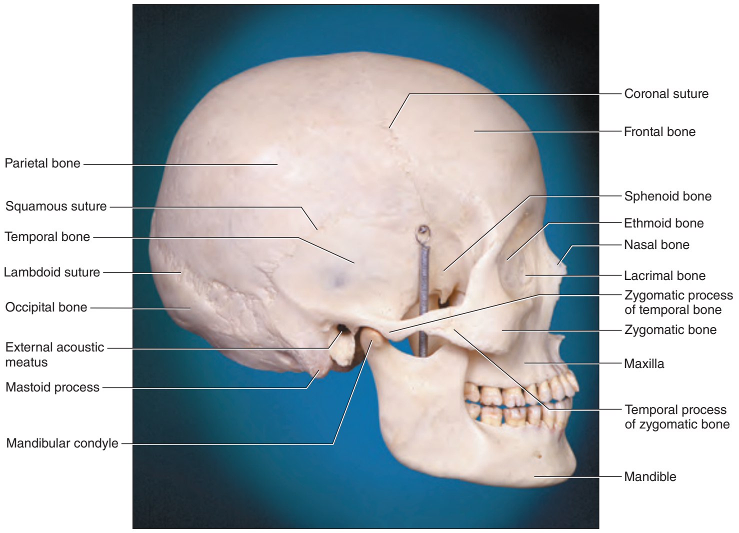
Discovery of the most common *CFTR* mutation in 1989 enabled development of more-targeted treatments. Thirty drugs are now in development. The new drugs work in various ways: correcting misfolded *CFTR* protein, restoring liquid on airway surfaces, breaking up mucus, improving nutrition, and fighting inflammation and infection.

Life with severe CF is challenging. In summertime, a child must avoid water from hoses, which harbor lung-loving *Pseudomonas* bacteria. Cookouts spew lung-irritating particulates. Too much chlorine in pools irritates lungs, whereas too little invites bacterial infection. New infections arise, too. In the past few years, multidrug-resistant *Mycobacterium abscessus*, related to the pathogen that causes tuberculosis, has affected 3% to 10% of CF patients in the United States and Europe.

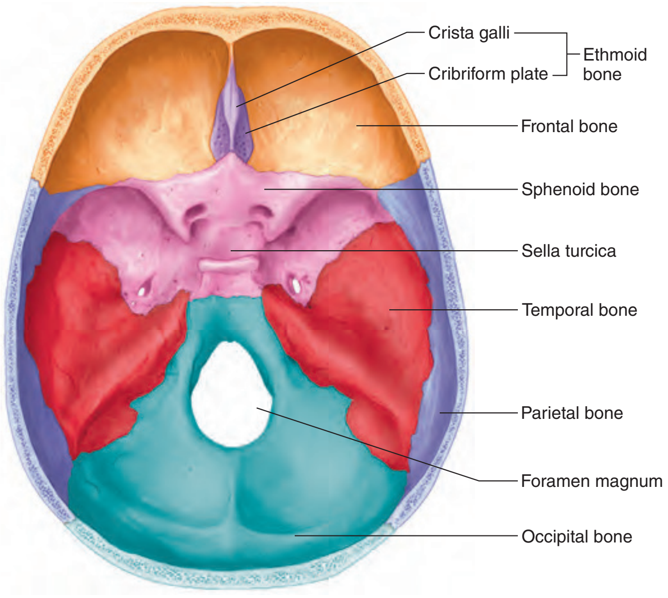
Remember when you were very young and presented with a substantial book for the first time? You were likely intimidated by its length, but were reassured that there were "a lot of pictures." This book has many "pictures" (figures) too, all designed to help you master the material. Some of the figure legends are followed by a question pertaining to that figure, intended to reinforce a concept or usage of terminology.

### *Photographs and Line Art*

Photographs provide a realistic view of anatomy.

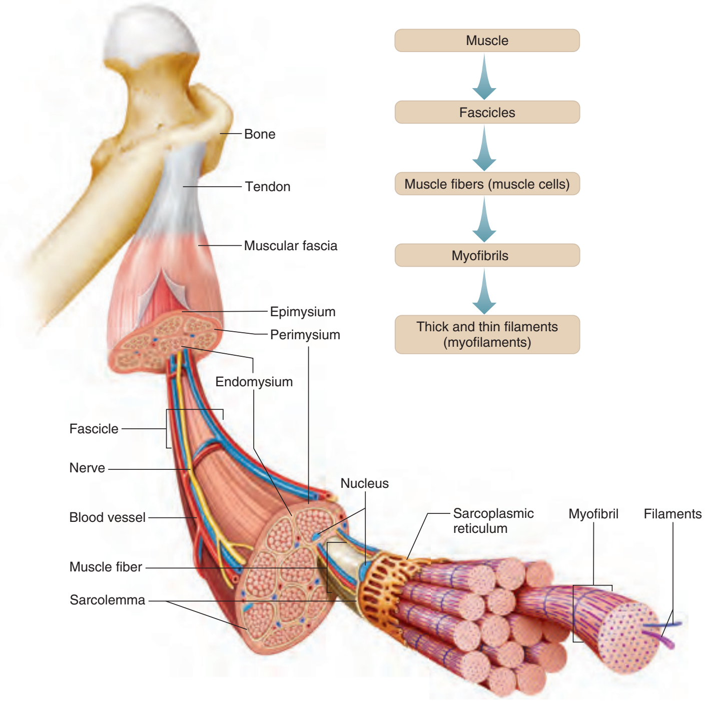

Coronal suture
Frontal bone
Parietal bone
Squamous suture
Temporal bone
Lambdoid suture
Occipital bone
External acoustic meatus
Mastoid process
Mandibular condyle
Sphenoid bone
Ethmoid bone
Nasal bone
Lacrimal bone
Zygomatic process of temporal bone
Zygomatic bone
Maxilla
Temporal process of zygomatic bone
Mandible

Line art can present different positions, layers, or perspectives.


Crista galli
Cribriform plate
Ethmoid bone
Frontal bone
Sphenoid bone
Sella turcica
Temporal bone
Parietal bone
Foramen magnum
Occipital bone

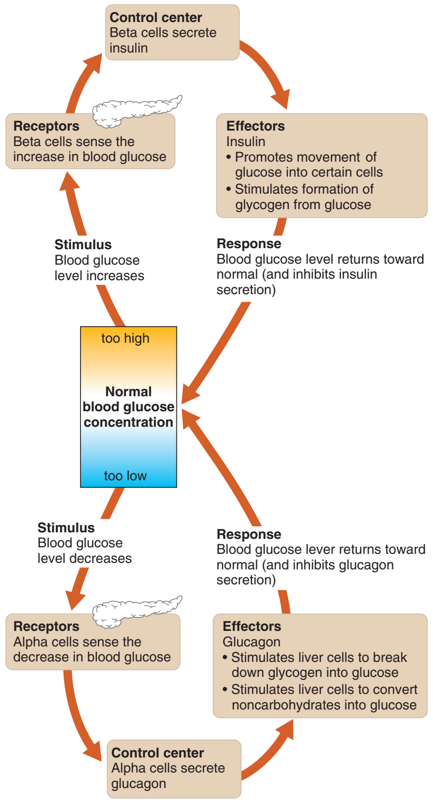
## *Macroscopic to Microscopic*

Many figures show anatomical structures in a manner that is macroscopic to microscopic (or vice versa).


Muscle
Fascicles
Muscle fibers (muscle cells)
Myofibrils
Thick and thin filaments (myofilaments)
Bone
Tendon
Muscular fascia
Epimysium
Perimysium
Endomysium
Fascicle
Nerve
Blood vessel
Muscle fiber
Sarcolemma
Nucleus
Sarcoplasmic reticulum
Myofibril
Filaments

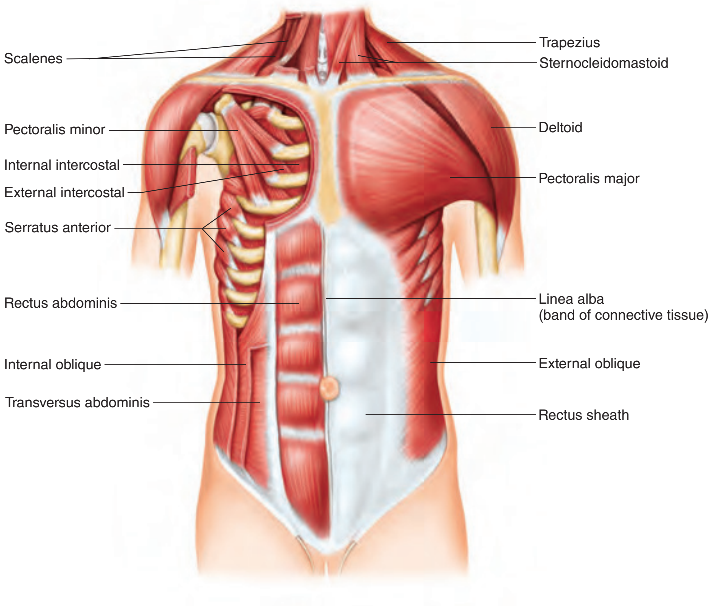
## *Flow Charts*

Flow charts depict sequences of related events, steps of pathways, and complex concepts, easing comprehension. Other figures may show physiological processes.

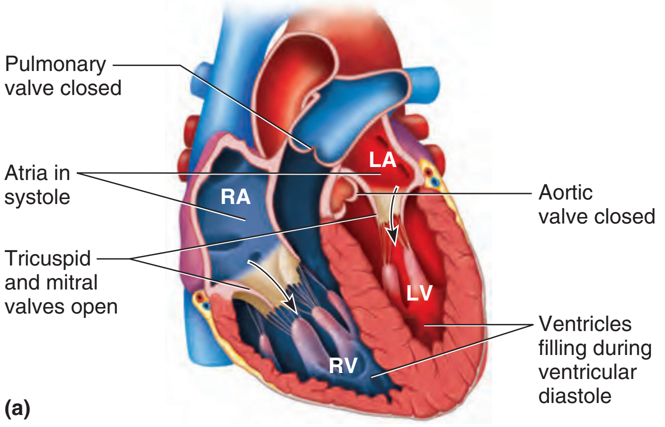

Control center
Beta cells secrete insulin
Effectors
Insulin
• Promotes movement of glucose into certain cells
• Stimulates formation of glycogen from glucose
Receptors
Beta cells sense the increase in blood glucose
Stimulus
Blood glucose level increases
Response
Blood glucose level returns toward normal (and inhibits insulin secretion)
too high
Normal blood glucose concentration
too low
Stimulus
Blood glucose level decreases
Response
Blood glucose lever returns toward normal (and inhibits glucagon secretion)
Receptors
Alpha cells sense the decrease in blood glucose
Effectors
Glucagon
• Stimulates liver cells to break down glycogen into glucose
• Stimulates liver cells to convert noncarbohydrates into glucose
Control center
Alpha cells secrete glucagon

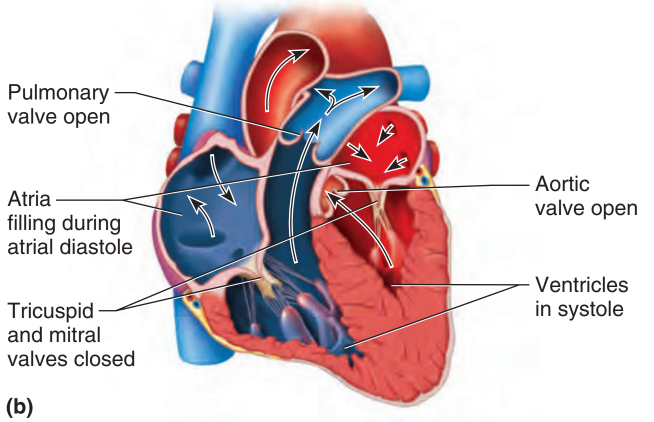
## *Anatomical Structures*

Some figures illustrate the locations of anatomical structures.


Scalenes
Pectoralis minor
Internal intercostal
External intercostal
Serratus anterior
Rectus abdominis
Internal oblique
Transversus abdominis
Trapezius
Sternocleidomastoid
Deltoid
Pectoralis major
Linea alba
(band of connective tissue)
External oblique
Rectus sheath

Other figures illustrate the functional relationships of anatomical structures.


Pulmonary valve closed
Atria in systole
Tricuspid and mitral valves open
LA
RA
LV
RV
Aortic valve closed
Ventricles filling during ventricular diastole
(a)


Pulmonary valve open
Atria filling during atrial diastole
Tricuspid and mitral valves closed
Aortic valve open
Ventricles in systole
(b)

### *Organizational Tables*

Organizational tables can help "put it all together," but are not a substitute for reading the text or having good notes.

**TABLE 5.6** **Muscle and Nervous Tissues**

| Type | Function | Location |
|---|---|---|
| Skeletal muscle tissue (striated) | Voluntary movements of skeletal parts | Muscles usually attached to bones |
| Smooth muscle tissue (lacks striations) | Involuntary movements of internal organs | Walls of hollow internal organs |
| Cardiac muscle tissue (striated) | Heart movements | Heart muscle |
| Nervous tissue | Sensory reception and conduction of electrical impulses | Brain, spinal cord, and peripheral nerves |

It is critical that you attend class regularly, and be on time—even if the instructor's notes are posted on the Web, and the information is in the textbook. For many learners, hearing and writing new information is a better way to retain facts than just scanning notes on a computer screen. Attending lectures and discussion sections also provides more detailed and applied analysis of the subject matter, as well as a chance to ask questions.

## During Class

Be alert and attentive in class. Take notes by adding to either the outline or notes taken while reading. Auditory learners benefit from recording the lectures and listening to them while driving or doing chores. This is called **multitasking**—doing more than one activity at a time.

Participate in class discussions, asking questions of the instructor and answering questions he or she poses. All of the students are in the class to learn, and many will be glad someone asked a question others would not be comfortable asking. Such student response can alert the instructor to topics that are misunderstood or not understood at all. However, respect class policy. Due to time constraints and class size, asking questions may be more appropriate after a large lecture class or during tutorial (small group) sessions.

## After Class

In learning complex material, expediency is critical. Organize, edit, and review notes as soon after class as possible, fleshing out sections where the lecturer got ahead of the listener. Highlighting or underlining (in color, for visual learners) the key terms, lists, important points, and major topics make them stand out, which eases both daily reviews and studying for exams.

### *Lists*

Organizing information into lists or categories can minimize information overload, breaking it into manageable chunks. For example, when studying the muscles of the thigh it is easier to learn the insertion, origin, action, and nerve supply of the four muscles making up the quadriceps femoris as a group, because they all have the same insertion, action, and nerve supply . . . they differ only in their origins.

### *Mnemonic Devices*

Another method for remembering information is the **mnemonic device.** One type of mnemonic device is a list of words, forming a phrase, in which the first letter of each word corresponds to the first letter of each word that must be remembered. For example, ***Frequent parades often test soldiers' endurance*** stands for the skull bones **f**rontal, **p**arietal, **o**ccipital, **t**emporal, **s**phenoid, and **e**thmoid. Another type of mnemonic device is a word formed by the first letters of the items to be remembered. For example, ***ipmat*** represents the stages in the cell cycle: **i**nterphase, **p**rophase, **m**etaphase, **a**naphase, and **t**elophase. Be inventive, develop mnemonic devices that you find helpful!

### *Study Groups*

Forming small study groups helps some students. Together the students review course material and compare notes. Working as a team and alternating leaders allows students to verbalize the information. Individual students can study and master one part of the assigned material, and then explain it to the others in the group, which incorporates the information into the memory of the speaker. Hearing the material spoken aloud also helps the auditory learner. Be sure to use anatomical and physiological terms, in explanations and everyday conversation, until they become part of your working vocabulary, rather than intimidating jargon. Most important of all—the group must stay on task, and not become a vehicle for social interaction. Your instructor may have suggestions or guidelines for setting up study groups.

### *Flash Cards*

Flash cards may seem archaic in this computer age, but they are still a great way to organize and master complex and abundant information. The act of writing or drawing on a note card helps the tactile learner. Master a few new cards each day and review cards from previous days, then use them all again at the end of the semester to prepare for the comprehensive final exam. They may even come in handy later, such as in studying for exams for admission to medical school or graduate school. Divide your deck in half and flip half of the cards so that the answer rather than the question is showing. Mix and shuffle them. Get used to identifying a structure or process from a description as well as giving a description when provided with a process or structure. This is more like what will be expected of you in the real world of the health-care professional.

### *Manage Your Time*

For each hour in the classroom, most students will spend at least three hours outside of class studying. Many of you have important obligations outside of class, such as jobs and family responsibilities. As important as these are, you still need to master this material on your path to becoming a health-care professional. Good time management skills are therefore essential in your study of human anatomy and physiology. In addition to class, lab, and study time, multitask. Spend time waiting for a ride or waiting in a doctor's office online reviewing notes or reading the text.

Daily repetition is helpful, so scheduling several short study periods each day should replace an end-of-semester crunch to cram for an exam. This does not take the place of time spent to prepare for the next class. Thinking about these suggestions for learning now can maximize study time throughout the semester, and, hopefully, lead to academic success. A working knowledge of the structure and function of the human body provides the foundation for all careers in the health sciences.

### PRACTICE

3. Why is it important to prepare before attending class?
4. Name two ways to participate in class discussions.
5. List several aids for remembering information.

## Summary Outline

A summary of the chapter provides an outline to review major ideas and is a tool for organizing thoughts.

**P.1 Introduction (page 2)**

*Try a variety of methods to study the human body.*

**P.2 Strategies for Your Success (page 2)**

*While strategies for academic success seem to be common sense, you might benefit from reminders of study methods.*

1. Before class
   Read the assigned text material prior to the corresponding class meeting.
   a. Photographs give a realistic view and line art shows different perspectives.
   b. Figures depicting macroscopic to microscopic show increase in detail.
   c. Flow charts depict sequences and steps.
   d. Figures of anatomical structures show locations.
   e. Organizational charts/tables summarize text.
2. During class
   Take notes and participate in class discussions.
3. After class
   a. Organize, edit, and review class notes.
   b. Mnemonic devices aid learning.
      (1) The first letters of the words you want to remember begin words of an easily recalled phrase.
      (2) The first letters of the items to be remembered form a word.
   c. Small study groups reviewing and vocalizing material can divide and conquer the learning task.
   d. Making flash cards helps the tactile learner.
   e. Time management skills encourage scheduled studying, including daily repetition instead of cramming for exams.

## CHAPTER ASSESSMENTS

Chapter assessments that are tied directly to the learning outcomes allow you to assess your mastery of the material. (Note the purple assess arrow.)

**P.1 Introduction**

1. Explain why the study of the human body can be overwhelming. (p. 2)

**P.2 Strategies for Your Success**

2. Methods to prepare for class include ______________ . (pp. 2–3)
   a. reading the chapter
   b. outlining the chapter
   c. making a vocabulary list
   d. all of the above
3. Describe how you can participate in class discussions. (p. 6)
4. Forming the phrase "I passed my anatomy test" to remember the cell cycle (interphase, prophase, metaphase, anaphase, telophase) is a ______________ device. (p. 6)
5. Name a benefit and a drawback of small study groups. (p. 6)
6. Give an example of effective time management used in preparation for success in the classroom. (p. 7)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

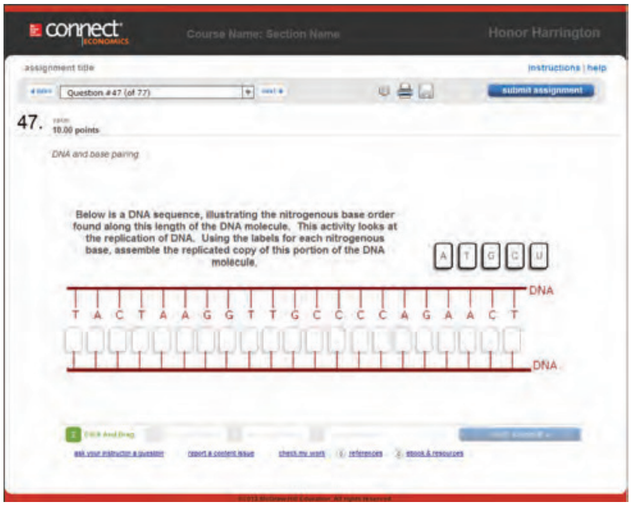
A textbook is inherently linear. This text begins with Chapter 1 and ends with Chapter 20. Understanding physiology and the significance of anatomy, however, requires you to be able to recall previous concepts. Critical thinking is all about linking previous concepts with current concepts under novel circumstances, in new ways. Toward this end, we have included in the Integrative Assessments/Critical Thinking section references to sections from earlier chapters. Making connections is what it is all about!

### OUTCOME P.1, P.2

1. Which study methods are most successful for you?

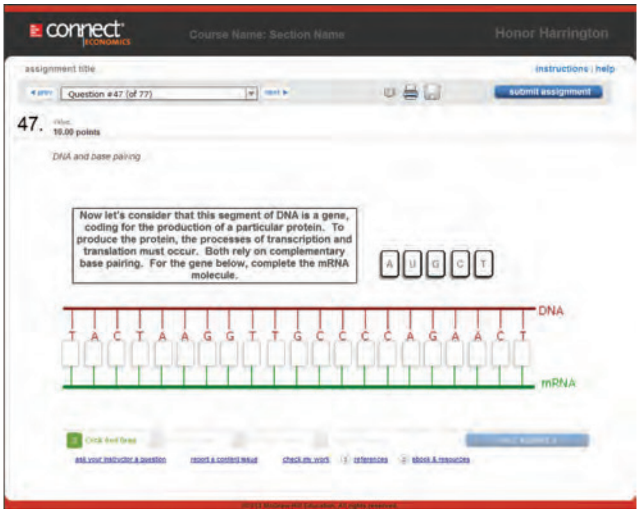
Check out McGraw-Hill online resources that can help you practice and assess your learning.

**Connect Interactive Questions** Reinforce your knowledge using assigned interactive questions.


connect
ECONOMICS
Course Name: Section Name
Honor Harrington
assignment title
instructions | help
Question #47 (of 77)
submit assignment
47.
10.00 points
DNA and base pairing
A
T
G
C
U
DNA
T A C T A A G G T T G C C C C A G A A C T
DNA
ask your instructor a question
report a content issue
check my work
references
ebook & resources

Below is a DNA sequence, illustrating the nitrogenous base order found along this length of the DNA molecule. This activity looks at the replication of DNA. Using the labels for each nitrogenous base, assemble the replicated copy of this portion of the DNA molecule.

**Connect Integrated Activity** Practice your understanding.

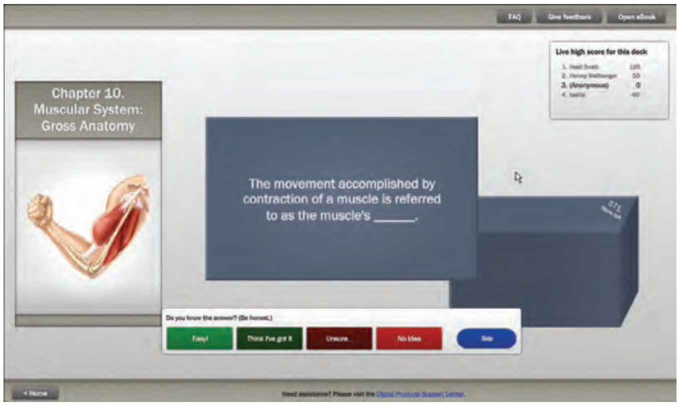

connect
ECONOMICS
Course Name: Section Name
Honor Harrington
assignment title
instructions | help
Question #47 (of 77)
submit assignment
47.
10.00 points
DNA and base pairing
A
U
G
C
T
DNA
T A C T A A G G T T G C C C C A G A A C T
mRNA
ask your instructor a question
report a content issue
check my work
references
ebook & resources

Now let's consider that this segment of DNA is a gene, coding for the production of a particular protein. To produce the protein, the processes of transcription and translation must occur. Both rely on complementary base pairing. For the gene below, complete the mRNA molecule.

### OUTCOMES P.2

2. Design a personalized study schedule.

**Learn Smart** Discover which concepts you have mastered and which require more attention with this personalized, adaptive learning tool.


FAQ
Give feedback
Open eBook
Live high score for this deck
Chapter 10.
Muscular System:
Gross Anatomy
Do you know the answer? (Be honest.)
Easy!
Think I've got it
Unsure...
No idea
Skip
< Home

The movement accomplished by contraction of a muscle is referred to as the muscle's ______.

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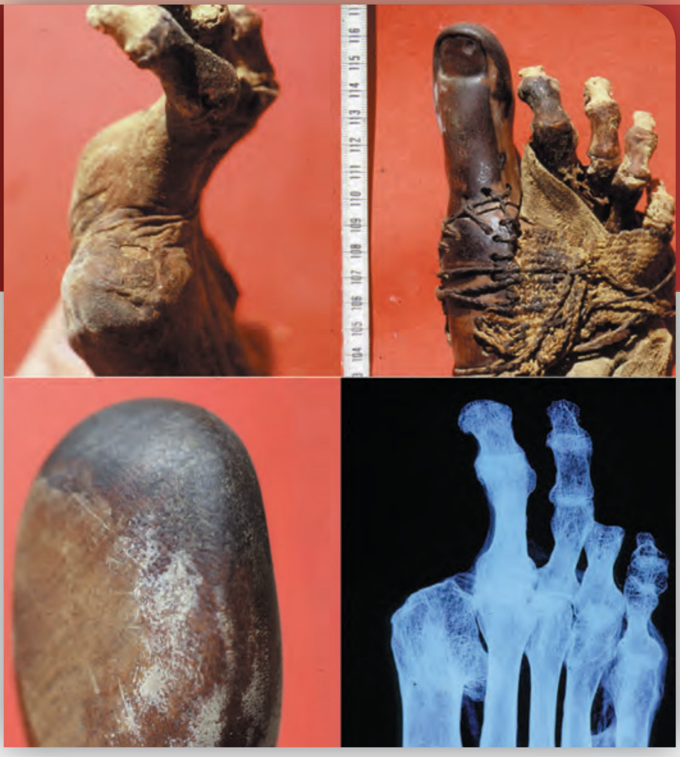
# 1

# Introduction to Human Anatomy and Physiology



*A wooden toe on an ancient Egyptian mummy reveals sophisticated knowledge of human anatomy and physiology from long ago.*

The mummy's toe. She lived between 1069 and 664 B.C. in Thebes, a city in ancient Egypt. Only pieces of her skeleton remain, held in place with plaster, glue, and linen. Yet, the telltale bones reveal a little of what her life was like.

The shape of the pelvic bones indicates that the person was female. She was 50 to 60 years old when she died, according to the way the bony plates of her skull fit together and the lines of mineral deposition in a well-preserved tooth. Among the preserved bones from the skull, pelvis, upper limbs, and right lower limb, the right big toe stands out, for it ends in a prosthesis, a manufactured replacement for a skeletal part. Was it purely cosmetic, or did it work?

The mummy's toe tip is wooden and painted a dark brown, perhaps to blend in with her skin color. A long part and two smaller parts anchor the structure to the stump. Seven leather strings once attached it to the foot, and it even bears a fake nail. Connective tissue and skin grew over the prosthesis, revealing that her body had accepted the replacement part, and the shape of the prosthesis was remarkably like that of a real toe. Signs of wear indicate that it was indeed used. Modern-day scientists made replicas of the toe and volunteers who were missing the same toe tried them out, demonstrating that the mummy's toe must have been crucial for balance and locomotion.

The replacement toe is evidence of sophisticated medical technology. Modern-day medical sleuths obtained computerized tomography (CT) scans of the remnants of the mummy. They detected poor mineral content in the toe, plus calcium deposits in the largest blood vessel, the aorta, suggesting impaired circulation to the feet. Perhaps the mummy in life suffered from diabetes mellitus, which can impede circulation to the toes. If gangrene had set in, healers might have amputated the affected portion of the toe, replacing it with a very reasonable facsimile.

The ancient Egyptians made other replacement parts, including ears, noses, feet, and lower limbs. Today prosthetic toes are made of silicones, which are plastic-like materials. People use them who have lost digits to injury, cancer, or, perhaps like the ancient Egyptian woman, diabetes.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 1.1 Introduction

1. Identify some of the early discoveries that led to our understanding of the body. (p. 10)

### 1.2 Anatomy and Physiology

2. Explain how anatomy and physiology are related. (p. 11)

### 1.3 Levels of Organization

3. List the levels of organization in the human body and the characteristics of each. (p.12)

### 1.4 Characteristics of Life

4. List and describe the major characteristics of life. (p. 13)
5. Give examples of metabolism. (p. 13)

### 1.5 Maintenance of Life

6. List and describe the major requirements of organisms. (pp. 13–14)
7. Explain the importance of homeostasis to survival. (p. 14)
8. Describe the parts of a homeostatic mechanism and explain how they function together. (pp. 14–15)

**1.6 Organization of the Human Body**

9. Identify the locations of the major body cavities. (pp. 16–17)
10. List the organs located in each major body cavity. (p. 17)
11. Name and identify the locations of the membranes associated with the thoracic and abdominopelvic cavities. (pp. 17–19)
12. Name the major organ systems, and list the organs associated with each. (pp. 19–22)
13. Describe the general functions of each organ system. (pp.19–22)

**1.7 Anatomical Terminology**

14. Properly use the terms that describe relative positions, body sections, and body regions. (p. 23)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**append-** [to hang something] *append*icular: Pertaining to the limbs.

**cardi-** [heart] peri*cardi*um: Membrane that surrounds the heart.

**cran-** [helmet] *cran*ial: Pertaining to the portion of the skull that surrounds the brain.

**dors-** [back] *dors*al: Position toward the back.

**homeo-** [same] *homeo*stasis: Maintenance of a stable internal environment.

**-logy** [study of] physio*logy*: Study of body functions.

**meta-** [change] *meta*bolism: Chemical changes in the body.

**pariet-** [wall] *pariet*al membrane: Membrane that lines the wall of a cavity.

**pelv-** [basin] *pelv*ic cavity: Basin-shaped cavity enclosed by the pelvic bones.

**peri-** [around] *peri*cardial membrane: Membrane that surrounds the heart.

**pleur-** [rib] *pleur*al membrane: Membrane that encloses the lungs and lines the thoracic cavity.

**-stasis** [standing still] homeo*stasis*: Maintenance of a stable internal environment.

**-tomy** [cutting] ana*tomy*: Study of structure, which often involves cutting or removing body parts.

---

## 1.1 | Introduction

Modern medicine began with long-ago observations on the function, and malfunction, of the human body. The study of the human body likely began when our early ancestors became curious about how their bodies worked, as we are today. At first they probably thought mostly about injuries and illnesses, because healthy bodies demand little attention from their owners. Early healers relied heavily on superstitions and notions about magic. However, as healers tried to help the sick, they began to discover useful ways of examining and treating the human body. They observed the effects of injuries, noticed how wounds healed, and examined cadavers to determine causes of death. They also found that certain herbs and potions could relieve coughs, headaches, fevers, and other common indications of illness.

Over time, people began to believe that humans could understand forces that caused natural events. They began observing the world around them more closely, asking questions and seeking answers. This set the stage for the development of modern medical science.

As techniques for making accurate observations and performing careful experiments evolved, knowledge of the human body expanded rapidly (fig. 1.1). At the same time, early medical providers coined many new terms to name body parts, describe their locations, and explain their functions and interactions. These terms, most of which originated from Greek and

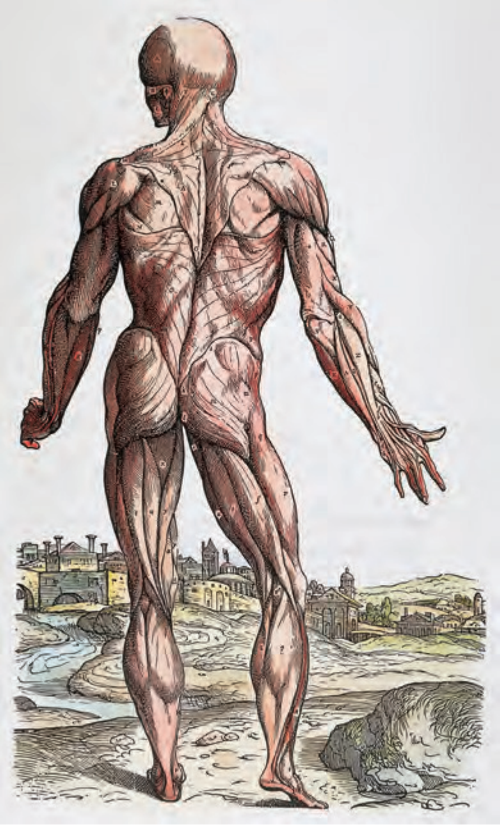


**FIGURE 1.1** The study of the human body has a long history, as evidenced by this illustration from the second book of *De Humani Corporis Fabrica* by Andreas Vesalius, issued in 1543. (Note the similarity to the anatomical position, described later in this chapter on page 23.)

Latin words, formed the basis for the language of anatomy and physiology that persists today. (The names of some modern medical and applied sciences are listed on pages 26–28.)

Much of what is known about the human body is based on *scientific method*, an approach to investigating the natural world. It is part of a general process called scientific inquiry. Scientific method consists of testing a hypothesis and then rejecting or accepting it, based on the results of experiments or observations. This method is described in greater detail in Appendix B, Scientific Method (p. 578), but it is likely that aspects of its application are already familiar to you. Imagine buying a used car. The dealer insists that the car is in fine shape, but you discover that the engine doesn't start. That's an experiment! It tests the hypothesis: If this car is in good shape, then it will start. When the car doesn't start, the wary consumer rejects the hypothesis and doesn't buy the car.

Rather than giving us all the answers, science eliminates wrong explanations. Our knowledge of the workings of the human body reflects centuries of asking questions, and testing, rejecting, and sometimes accepting hypotheses. New technologies provide new views of anatomy and physiology, so that knowledge is always growing. One day you may be the one to discover something previously unknown about the human body!

**PRACTICE**

1. What factors probably stimulated an early interest in the human body?
2. What kinds of activities helped promote the development of modern medical science?

## 1.2 | Anatomy and Physiology

**Anatomy** (ah-nat′o-me) is the branch of science that deals with the structure (morphology) of body parts—their forms and how they are organized. **Physiology** (fiz″e-ol′o-je), on the other hand, concerns the functions of body parts—what they do and how they do it.

The topics of anatomy and physiology are difficult to separate because the structures of body parts are so closely associated with their functions. Body parts form a well-organized unit—the human organism—and each part functions in the unit's operation. A particular body part's function depends on the way the part is constructed—that is, how its subparts are organized. For example, the organization of the parts in the human hand with its long, jointed fingers makes it easy to grasp objects; the hollow chambers of the heart are adapted to pump blood through tubular blood vessels; the shape of the mouth enables it to receive food; and teeth are shaped to break solid foods into small pieces (fig. 1.2).

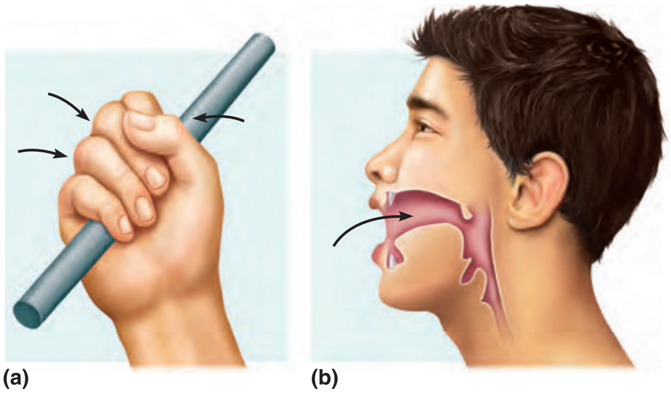


**FIGURE 1.2** The structures of body parts make possible their functions: **(a)** The hand is adapted for grasping, **(b)** the mouth for receiving food. (Arrows indicate movements associated with these functions.)

As ancient as the fields of anatomy and physiology are, we are always learning more. For example, researchers recently used imaging technology to identify a previously unrecognized part of the brain, the planum temporale, which enables people to locate sounds in space. Many discoveries today begin with

CAREER CORNER

### Emergency Medical Technician

The driver turns a corner and suddenly swerves as a cat dashes into the road. She slams on the brakes but hits a parked car, banging her head against the steering wheel. Onlookers call 911, and within minutes an ambulance drives up.

The driver of the ambulance and another emergency medical technician (EMT) leap out and run over to the accident scene. They open the driver side door and quickly assess the woman's condition by evaluating her breathing, taking her blood pressure and pulse. She is bleeding from a laceration on her forehead, and is conscious but confused.

The EMTs carefully place a restraint at the back of her neck and move her onto a board, then slide her into the ambulance. While one EMT drives, the other rides in the back with the patient and applies pressure to the cut. At the hospital, the EMTs document the care provided and clean and restock the ambulance.

EMTs care for ill or injured people in emergency situations and transport patients, such as from a hospital to a nursing home. The work is outside and inside and requires quick thinking as well as strength. Requirements vary by state, but all EMTs must be licensed. Basic EMTs take 120–150 hours of training; paramedic EMTs take 1200–1800 hours of training. Paramedics may give injections, set up intravenous lines, and give more medications than can basic EMTs.

investigations at the molecular or cellular level. In this way, researchers have discovered that certain cells in the small intestine bear the same taste receptor proteins found on the tongue. At both locations, the receptors detect molecules of sugar. The cells in the tongue provide taste sensations, whereas the cells in the intestines help regulate the digestion of sugar. The discovery of the planum temporale is anatomical; the discovery of sweet receptors in the intestine is physiological.

By discovering which of our 20,500 or so genes are active in particular diseases, researchers are finding commonalities among illnesses that are not apparent on the whole-body level. These findings suggest new targets for drugs—both new ones and "repurposed" drugs that are already available.

**PRACTICE**

3. Why is it difficult to separate the topics of anatomy and physiology?
4. List examples that illustrate how the structure of a body part makes possible its function.

## 1.3 | Levels of Organization

Until the invention of magnifying lenses and microscopes about 400 years ago, anatomists were limited in their studies to what they could see with the unaided eye—large parts. But with these new tools, investigators discovered that larger body structures are made up of smaller parts, which in turn are composed of even smaller ones.

Figure 1.3 shows the levels of organization that modern-day scientists recognize. All materials, including those that make up the human body, are composed of chemicals. Chemicals consist of microscopic particles called **atoms,** which join to form **molecules.** Small molecules can combine in complex ways to form larger **macromolecules.**

In the human and other organisms, the basic unit of structure and function is a **cell,** which is microscopic. Although cells vary in size, shape, and specialized functions, all share certain characteristics. For instance, all cells of humans and other complex organisms contain structures called **organelles** (or″gah-nelz′) that carry out specific activities. Organelles are composed of aggregates of macromolecules, such as proteins, carbohydrates, lipids, and nucleic acids.

Cells may be organized into layers or other structures that have common functions. Such a group of

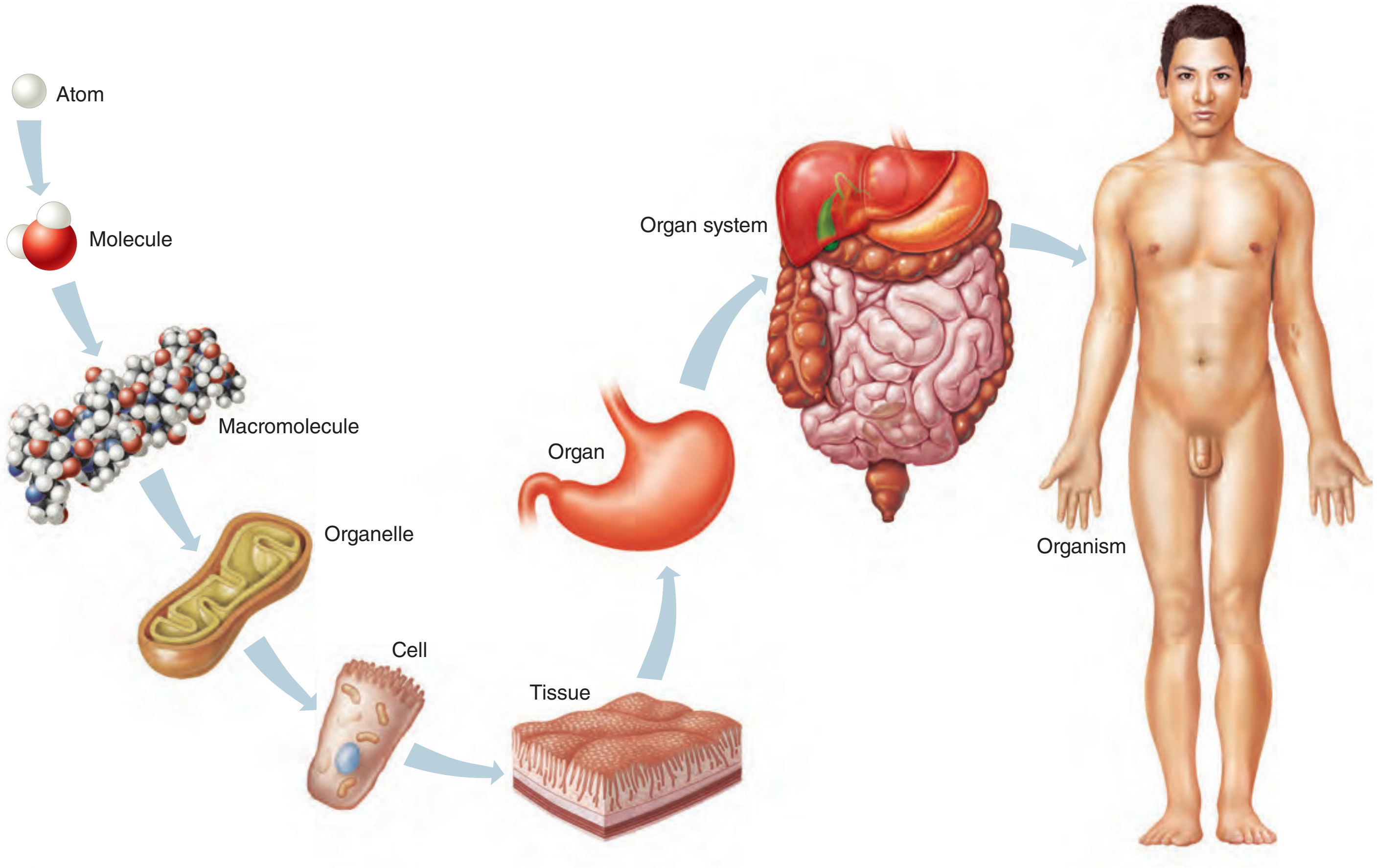


**FIGURE 1.3** A human body is composed of parts within parts, with increasing complexity.

cells forms a **tissue.** Groups of different tissues that interact form **organs**—complex structures with specialized functions—and groups of organs that function closely together compose **organ systems.** Organ systems make up an **organism** (or′gah-nizm), which is a living thing.

Body parts can be described in terms of different levels of organization, such as the *atomic level,* the *molecular level,* or the *cellular level.* Furthermore, body parts differ in complexity from one level to the next. That is, atoms are less complex than molecules, molecules are less complex than organelles, tissues are less complex than organs, and so forth.

Chapters 2–6 discuss these levels of organization in more detail. Chapter 2 describes the atomic and molecular levels. Chapter 3 deals with organelles and cellular structures and functions, and chapter 4 explores cellular metabolism. Chapter 5 describes tissues and presents membranes (linings) as examples of organs, and chapter 6 considers the skin and its accessory organs as an example of an organ system. The remaining chapters describe the structures and functions of each of the other organ systems in detail.

**PRACTICE**

5. How does the human body illustrate levels of organization?
6. What is an organism?
7. How do body parts at different levels of organization vary in complexity?

## 1.4 | Characteristics of Life

As living organisms, we can respond to our surroundings. Our bodies grow, eventually becoming able to reproduce. We gain energy by ingesting (taking in), digesting (breaking down), absorbing, and assimilating the nutrients in food. The absorbed substances circulate throughout the internal environment of our bodies. We can then, by the process of respiration, use the energy in these nutrients for such vital functions as movement, growth, and repair of tissues. Finally, we excrete wastes. Taken together, these physical and chemical events that obtain, release, and use energy are a major part of **metabolism** (mĕ-tab′o-liz-m), all of the chemical reactions in cells. Table 1.1 summarizes the characteristics of life.

**PRACTICE**

8. What are the characteristics of life?
9. How are the characteristics of life dependent on metabolism?

**TABLE 1.1 Characteristics of Life**

| Process | Examples |
|---|---|
| Movement | Change in position of the body or of a body part; motion of an internal organ |
| Responsiveness | Reaction to a change inside or outside the body |
| Growth | Increase in body size without change in shape |
| Reproduction | Production of new organisms and new cells |
| Respiration | Obtaining oxygen, removing carbon dioxide, and releasing energy from foods (Some forms of life do not use oxygen in respiration.) |
| Digestion | Breakdown of food substances into simpler forms that can be absorbed and used |
| Absorption | Passage of substances through membranes and into body fluids |
| Circulation | Movement of substances in body fluids |
| Assimilation | Changing absorbed substances into chemically different forms |
| Excretion | Removal of wastes produced by metabolic reactions |

## 1.5 | Maintenance of Life

The structures and functions of almost all body parts help maintain life. Even an organism's reproductive structures, whose primary function is to ensure that its species will continue into the future, may contribute to survival. For example, sex hormones help to strengthen bones.

### Requirements of Organisms

Being alive requires certain environmental factors, including the following:

1. **Water** is the most abundant chemical in the body. It is required for many metabolic processes and provides the environment in which most of them take place. Water also transports substances within the organism and is important in regulating body temperature. Water found inside the cells, along with substances dissolved in it, constitutes the intracellular fluid. Similarly, outside of the cells, including the tissue fluid and the liquid portion of the blood (plasma), is the extracellular fluid (fig. 1.4)
2. **Foods** are substances that provide the body with necessary chemicals (nutrients) in addition to water. Some of these chemicals are used as energy sources, others supply raw materials for building new living matter, and still others help regulate vital chemical reactions.

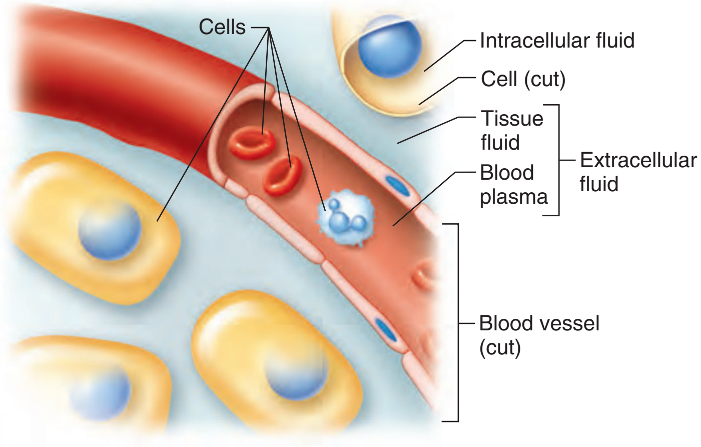


**FIGURE 1.4** Intracellular and extracellular fluids.

3. **Oxygen** is a gas that makes up about one-fifth of ordinary air. It is used to release energy from food substances. This energy, in turn, drives metabolic processes.
4. **Heat** is a form of energy. It is a product of metabolic reactions, and the degree of heat present partly determines the rate at which these reactions occur. Generally, the more heat, the more rapidly chemical reactions take place. (*Temperature* is a measure of the degree of heat.)
5. **Pressure** is an application of force to something. For example, the force on the outside of the body due to the weight of air above it is called *atmospheric pressure.* In humans, this pressure is important in breathing. Similarly, organisms living under water are subjected to *hydrostatic pressure*—a pressure a liquid exerts—due to the weight of water above them. In humans, heart action produces blood pressure (another form of hydrostatic pressure), which forces blood through blood vessels.

Health-care workers repeatedly monitor patients' *vital signs*—observable body functions that reflect essential metabolic activities. Vital signs indicate that a person is alive. Assessment of vital signs includes measuring body temperature and blood pressure and monitoring rates and types of pulse and breathing movements. Absence of vital signs signifies death. A person who has died displays no spontaneous muscular movements, including those of the breathing muscles and beating heart. A dead person does not respond to stimuli and has no reflexes, such as the knee-jerk reflex and the pupillary reflexes of the eye. Brain waves cease with death, as demonstrated by a flat electroencephalogram (EEG), which signifies a lack of metabolic activity in the brain.

Organisms require water, food, oxygen, heat, and pressure, but these alone are not enough to ensure survival. Both the quantities and the qualities of such factors are also important. For example, the volume of water entering and leaving an organism must be regulated, as must the concentration of oxygen in body fluids. Similarly, survival depends on the quality as well as the quantity of food available—that is, food must supply the correct nutrients in adequate amounts.

## Homeostasis

Factors in the external environment may change. If an organism is to survive, however, conditions within the fluid surrounding its body cells, which compose its **internal environment,** must remain relatively stable. In other words, body parts function only when the concentrations of water, nutrients, and oxygen and the conditions of heat and pressure remain within certain narrow limits. This condition of a stable internal environment is called **homeostasis** (ho″me-ō-sta′sis).

The body maintains homeostasis through a number of self-regulating control systems, or **homeostatic mechanisms,** that share the following three components (fig. 1.5):

- **Receptors** provide information about specific conditions (stimuli) in the internal environment.
- A **set point** tells what a particular value should be, such as body temperature at 37°C (Celsius) or 98.6°F (Fahrenheit). More about metric equivalents can be found in Appendix C (p. 579); metric units are used throughout this text.
- **Effectors** bring about responses that alter conditions in the internal environment.

A homeostatic mechanism works as follows. If the receptors measure deviations from the set point, effectors are activated that can return conditions toward normal. As conditions return toward normal, the deviation from the set point progressively lessens and the effectors are gradually shut down. Such a response is called a **negative feedback** (neg′ah-tiv fēd′bak) mechanism, both because the deviation from the set point is cor-

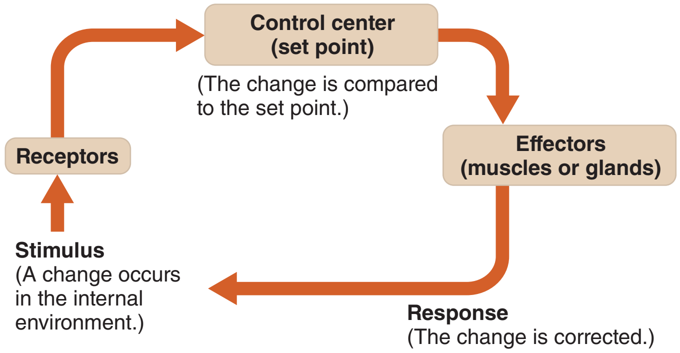

Control center
(set point)
(The change is compared to the set point.)
Effectors
(muscles or glands)
Response
(The change is corrected.)
Stimulus
(A change occurs in the internal environment.)
Receptors

**FIGURE 1.5** A homeostatic mechanism monitors a particular aspect of the internal environment and corrects any changes back to the value indicated by the set point.

rected (moves in the opposite or negative direction) and because the correction reduces the action of the effectors. This latter aspect is important because it prevents a correction from going too far.

To better understand the idea of negative feedback, imagine a room equipped with a furnace and an air conditioner (fig. 1.6). If the room temperature is to remain near 20°C (68°F), the thermostat is adjusted to an operating level, or set point, of 20°C. A thermostat, which senses temperature changes, signals the furnace to start and the air conditioner to stop whenever the room temperature drops below the set point. If the temperature rises above the set point, the thermostat stops the furnace and starts the air conditioner. As a result, the room maintains a relatively constant temperature.

Body temperature is regulated by a homeostatic mechanism that is similar to control of room temperature. Temperature receptors are scattered throughout the body. The "thermostat" is a temperature-sensitive region in a temperature control center of the brain. In healthy persons, the set point of the brain's thermostat is at or near 37°C (98.6°F).

If a person is exposed to cold and body temperature begins to drop, the temperature receptors sense this change and the temperature control center triggers heat-generating and heat-conserving activities. For example, small groups of muscles are stimulated to contract involuntarily, an action called *shivering.* Such muscular contractions produce heat, which helps warm the body. At the same time, blood vessels in the skin are signaled to constrict so that less warm blood flows through them. In this way, deeper tissues retain heat that might otherwise be lost.

If a person is becoming overheated, the brain's temperature control center triggers a series of changes that promote loss of body heat. Sweat glands in the skin secrete perspiration, and as this fluid evaporates from the surface, heat is carried away and the skin is cooled. At the same time, the brain center dilates blood vessels in the skin. This action allows the blood carrying heat from deeper tissues to reach the surface, where heat is lost to the outside (fig. 1.7). The brain stimulates an increase in heart rate, which sends a greater volume of blood into surface vessels, and an increase in breathing rate, which allows the lungs to expel more heat-carrying air. Body temperature regulation is discussed further in chapter 6 (pp. 135–136).

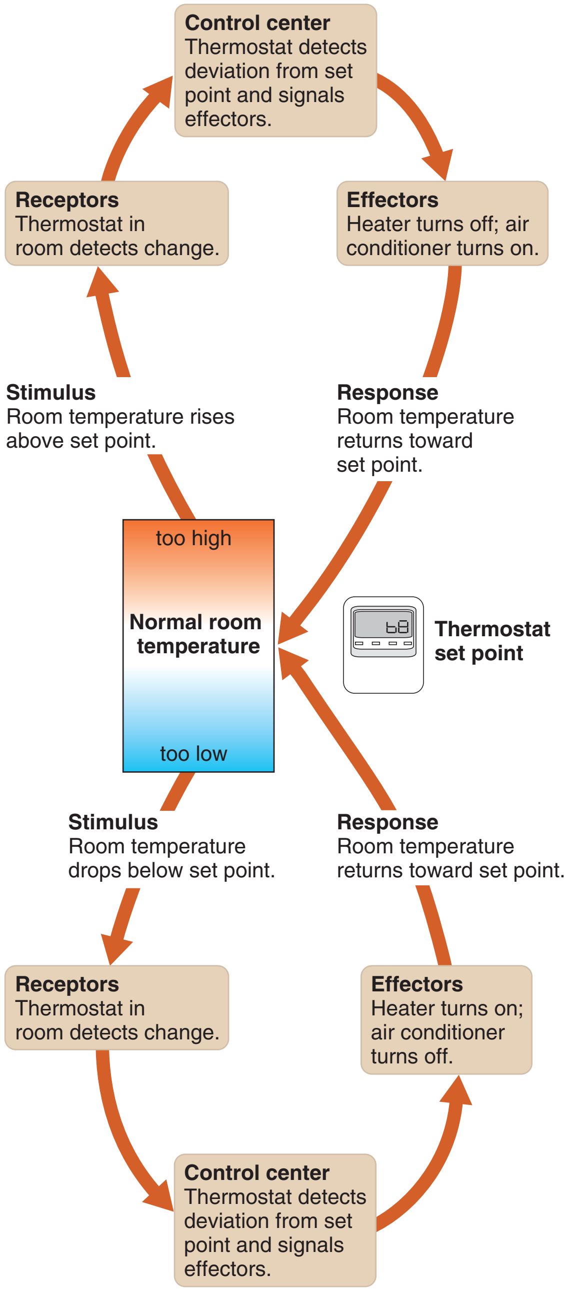

**Control center**
Thermostat detects deviation from set point and signals effectors.
**Receptors**
Thermostat in room detects change.
**Effectors**
Heater turns off; air conditioner turns on.
**Stimulus**
Room temperature rises above set point.
**Response**
Room temperature returns toward set point.
too high
**Normal room temperature**
too low
68
**Thermostat set point**
**Stimulus**
Room temperature drops below set point.
**Response**
Room temperature returns toward set point.
**Receptors**
Thermostat in room detects change.
**Effectors**
Heater turns on; air conditioner turns off.
**Control center**
Thermostat detects deviation from set point and signals effectors.

**FIGURE 1.6** A thermostat signals an air conditioner and a furnace to turn on or off to maintain a relatively stable room temperature. This system is an example of a homeostatic mechanism.

**Q** *What would happen to room temperature if the set point were turned up?*

**Answer can be found in Appendix F on page 582.**

Another homeostatic mechanism regulates the blood pressure in the blood vessels (arteries) leading away from the heart. Pressure-sensitive receptors in the walls of these vessels sense changes in blood pressure and signal a pressure control center in the brain. If blood pressure is above the set point, the brain signals the heart chambers to contract more slowly and with less force. This decreased heart action sends less blood into the blood vessels, decreasing the pressure inside them. If blood pressure falls below the set point, the brain center signals the heart to contract more rapidly and with greater force. As a result, the pressure in the vessels increases. Chapter 13 (pp. 370–371) discusses regulation of blood pressure in more detail.

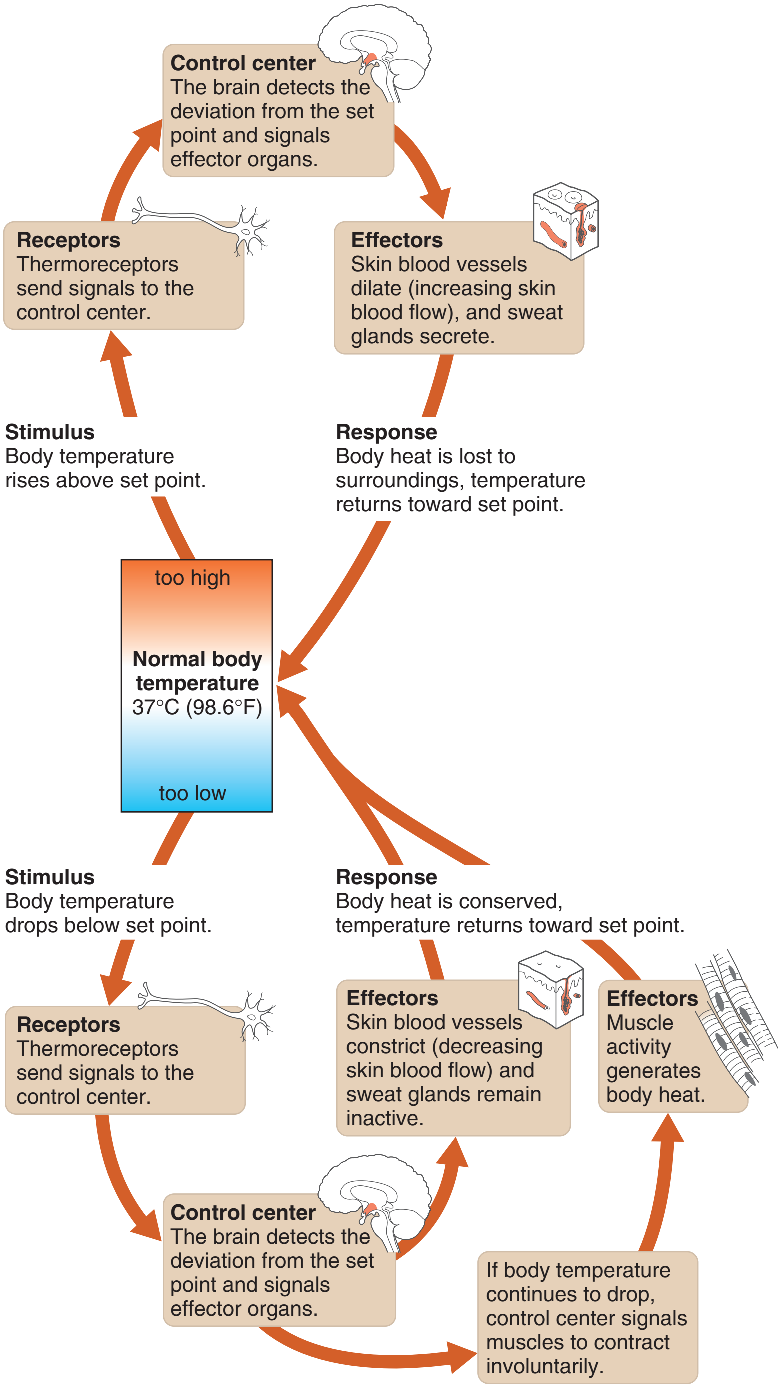

**Control center**
The brain detects the deviation from the set point and signals effector organs.
**Receptors**
Thermoreceptors send signals to the control center.
**Effectors**
Skin blood vessels dilate (increasing skin blood flow), and sweat glands secrete.
**Stimulus**
Body temperature rises above set point.
**Response**
Body heat is lost to surroundings, temperature returns toward set point.
too high
**Normal body temperature**
37°C (98.6°F)
too low
**Stimulus**
Body temperature drops below set point.
**Response**
Body heat is conserved, temperature returns toward set point.
**Receptors**
Thermoreceptors send signals to the control center.
**Effectors**
Skin blood vessels constrict (decreasing skin blood flow) and sweat glands remain inactive.
**Effectors**
Muscle activity generates body heat.
**Control center**
The brain detects the deviation from the set point and signals effector organs.
If body temperature continues to drop, control center signals muscles to contract involuntarily.

**FIGURE 1.7** A homeostatic mechanism regulates body temperature.

Human physiology offers many other examples of homeostatic mechanisms. All work by the same general process as the two preceding examples. Just as anatomical terms are used repeatedly throughout this book, so can the basic principles of a homeostatic mechanism be applied to the different organ systems. Homeostatic mechanisms maintain a relatively constant internal environment, yet physiological values may vary slightly in a person from time to time or from one individual to another. Therefore, both normal values for an individual and the *normal range* for the general population are clinically important.

Organ systems contribute to homeostasis in different ways. Resources brought in by the digestive and respiratory systems are delivered to all body cells by the cardiovascular system. The same blood that brings needed nutrients to cells carries away waste products, which are removed by the respiratory and urinary systems (fig. 1.8).

Most feedback mechanisms in the body are negative. However, sometimes change stimulates further change. A process that moves conditions away from the normal state is called a *positive feedback mechanism.* In blood clotting, for example, the chemicals that carry out clotting stimulate more clotting, minimizing bleeding (see chapter 12, p. 340). Another positive feedback mechanism increases the strength of uterine contractions during childbirth, helping to bring the new individual into the world (see chapter 20, pp. 564–565).

Positive feedback mechanisms usually produce unstable conditions, which might seem incompatible with homeostasis. However, the examples of positive feedback associated with normal health have very specific functions and are short-lived.

## PRACTICE

10. Which requirements of organisms does the external environment provide?
11. Why is homeostasis important to survival?
12. Describe two homeostatic mechanisms.

## 1.6 | Organization of the Human Body

The human organism is a complex structure composed of many parts. Its major features include several body cavities, layers of membranes within these cavities, and a variety of organ systems.

### Body Cavities

The human organism can be divided into an **axial** (ak′se-al) portion, which includes the head, neck, and trunk, and an **appendicular** (ap″en-dik′u-lar) portion, which includes the upper and lower limbs. Within the axial portion are the **cranial cavity,** which houses the brain; the **vertebral canal,** which contains the spinal cord within the sections of the backbone (vertebrae); the **thoracic** (tho-ras′ik) **cavity;** and the **abdominopelvic** (ab-dom″ĭ-no-pel′vik) **cavity.** The organs within these last two cavities are called **viscera** (vis′er-ah) (fig. 1.9*a*).

A broad, thin skeletal (voluntary) muscle called the **diaphragm** separates the thoracic cavity from the

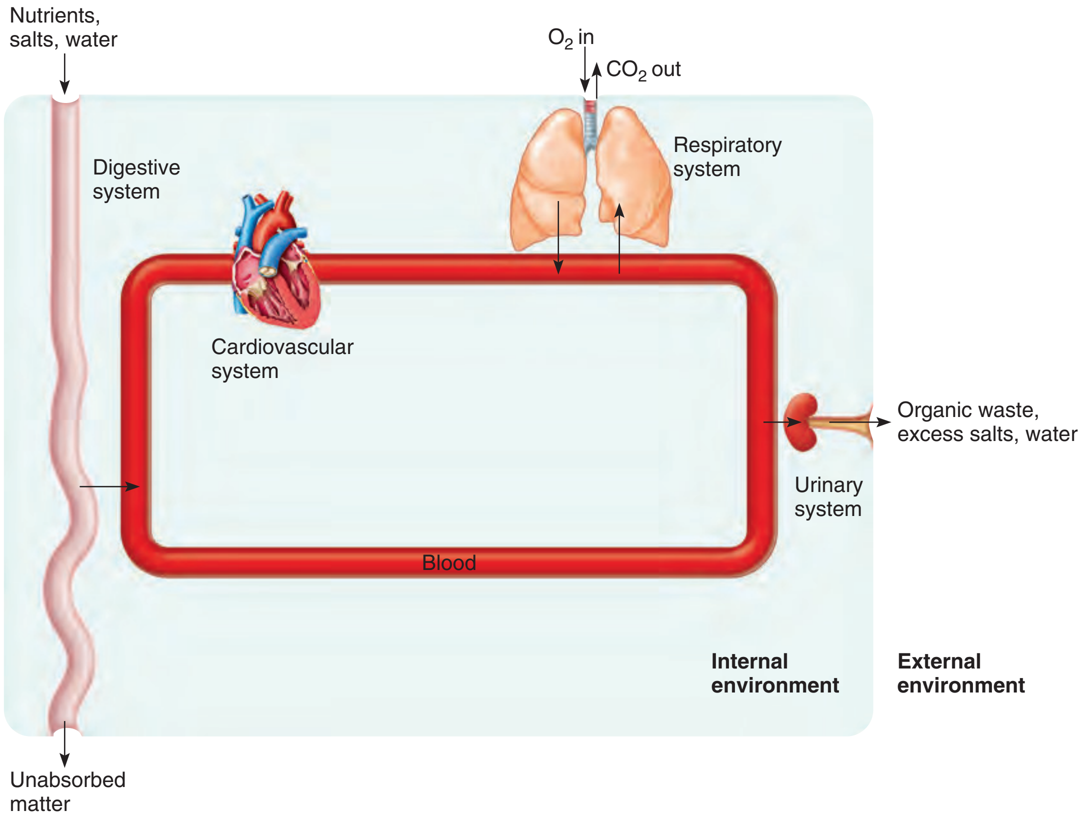


**FIGURE 1.8** Organ systems contribute to homeostasis. Concentrations of water, nutrients, and oxygen in the internal environment must be maintained within certain ranges to sustain life.

abdominopelvic cavity. The thoracic cavity wall is composed of skin, skeletal muscles, and various bones.

A region called the **mediastinum** (me″de-as-ti′num) separates the thoracic cavity into two compartments, which contain the right and left lungs. The remaining thoracic viscera—heart, esophagus, trachea, and thymus—are located within the mediastinum (fig. 1.9*b*).

The abdominopelvic cavity, which includes an upper abdominal portion and a lower pelvic portion, extends from the diaphragm to the floor of the pelvis. Its wall consists primarily of skin, skeletal muscles, and bones. The viscera within the **abdominal cavity** include the stomach, liver, spleen, gallbladder, kidneys, and most of the small and large intestines.

The **pelvic cavity** is the portion of the abdominopelvic cavity enclosed by the hip bones (see chapter 7, p. 168). It contains the terminal portion of the large intestine, the urinary bladder, and the internal reproductive organs.

Smaller cavities within the head include (fig. 1.10):

1. **Oral cavity,** containing the teeth and tongue.
2. **Nasal cavity,** located within the nose and divided into right and left portions by a nasal septum. Several air-filled *sinuses* connect to the nasal cavity (see chapter 7, pp. 155–157). These include the frontal and sphenoidal sinuses shown in figure 1.10.
3. **Orbital cavities,** containing the eyes and associated skeletal muscles and nerves.
4. **Middle ear cavities,** containing the middle ear bones.

## Thoracic and Abdominopelvic Membranes

The walls of the right and left thoracic compartments, which contain the lungs, are lined with a membrane called the *parietal pleura* (fig. 1.11). A similar membrane, called the *visceral pleura,* covers each lung. (Note: **Parietal** [pah-ri′ĕ-tal] refers to the membrane attached to the wall of a cavity; **visceral** [vis′er-al] refers to the membrane that is deeper—toward the interior—and covers an internal organ, such as a lung.)

The parietal and visceral **pleural membranes** (ploo′ral mem′brānz) are separated by a thin film of watery fluid (serous fluid), which they secrete. While no actual space normally exists between these membranes, the potential space between them is called the *pleural cavity* (see figs. 1.9*b* and 1.11).

The heart, which is located in the broadest portion of the mediastinum, is surrounded by **pericardial** (per″ĭ-kar′de-al) **membranes.** A *visceral pericardium* covers the heart's surface and is separated

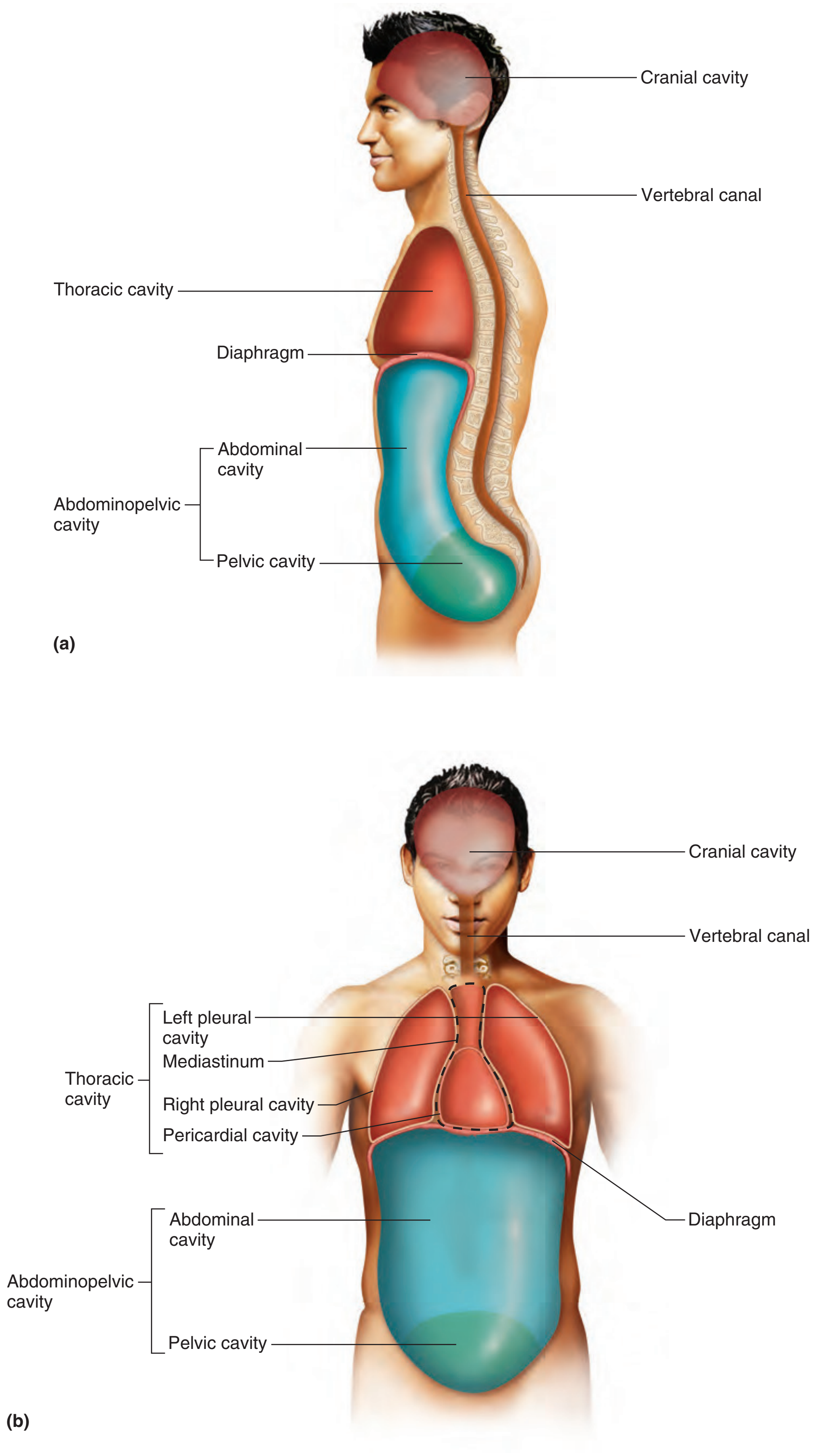

Cranial cavity
Vertebral canal
Thoracic cavity
Diaphragm
Abdominal cavity
Abdominopelvic cavity
Pelvic cavity
(a)
Cranial cavity
Vertebral canal
Left pleural cavity
Mediastinum
Thoracic cavity
Right pleural cavity
Pericardial cavity
Diaphragm
Abdominal cavity
Abdominopelvic cavity
Pelvic cavity
(b)

**FIGURE 1.9** APR Major body cavities. **(a)** Lateral view. **(b)** Anterior view.

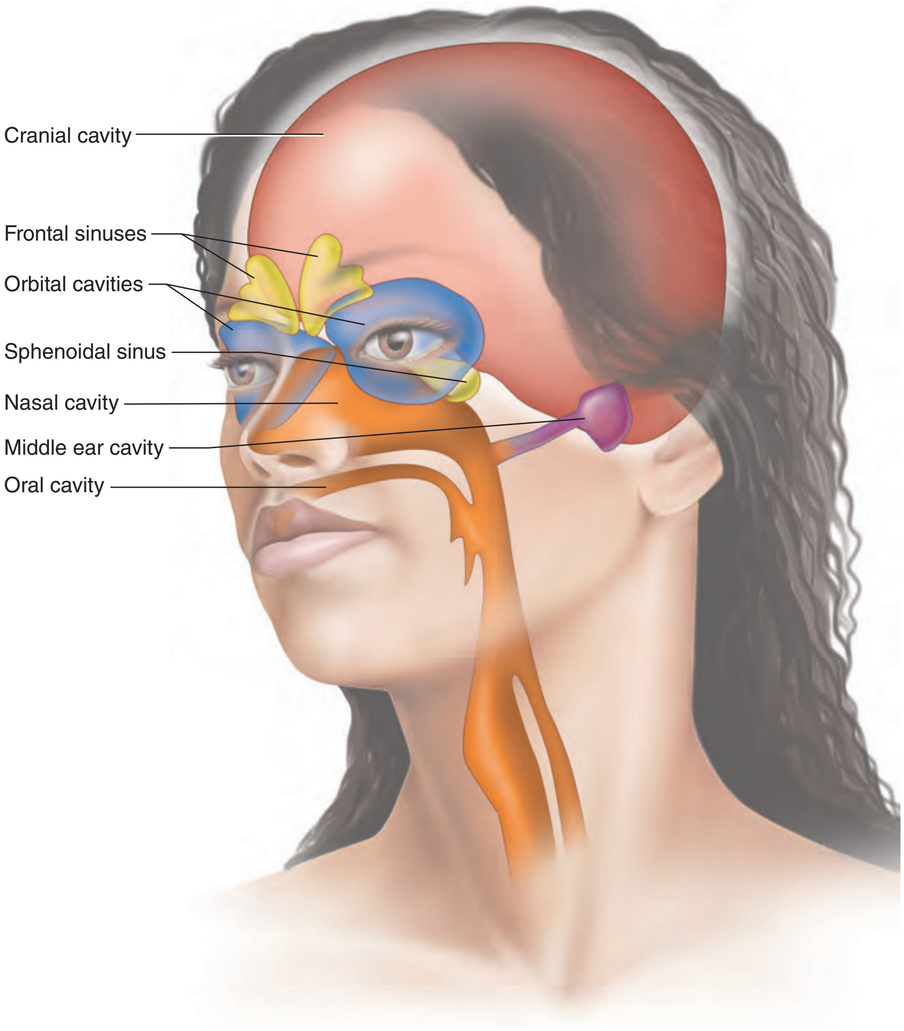


**FIGURE 1.10** The cavities within the head include the cranial, oral, nasal, orbital, and middle ear cavities, as well as several sinuses. (Not all of the sinuses are shown.)

from a *parietal pericardium* by a small volume of fluid. The *pericardial cavity* (see figs. 1.9*b* and 1.11) is the potential space between these membranes.

In the abdominopelvic cavity, the membranes are called **peritoneal** (per″ĭ-to-ne′al) **membranes.** A *parietal peritoneum* lines the wall, and a *visceral peritoneum* covers each organ in the abdominal cavity (fig. 1.12). The *peritoneal cavity* is the potential space between these membranes.

## PRACTICE

13. What does *viscera* mean?
14. Which organ occupies the cranial cavity? the vertebral canal?
15. Name the cavities of the head.
16. Describe the membranes associated with the thoracic and abdominopelvic cavities.

## Organ Systems

A human body consists of several organ systems. Each system includes a set of interrelated organs that work together to provide specialized functions that contribute to homeostasis (fig. 1.13). As you read about each system, you may want to consult the illustrations of the human torso in the Reference Plates (see pages 31–38) and locate some of the organs described. The following introduction to the organ systems is presented according to overall functions.

### *Body Covering*

Organs of the **integumentary** (in-teg-u-men′tar-e) **system** (see chapter 6) include the skin and various accessory organs, such as the hair, nails, sweat glands, and sebaceous glands. These parts protect underlying tissues, help regulate body temperature, house a variety of sensory receptors, and synthesize certain products.

**FIGURE 1.11** APR A transverse section through the thorax reveals the serous membranes associated with the heart and lungs (superior view).

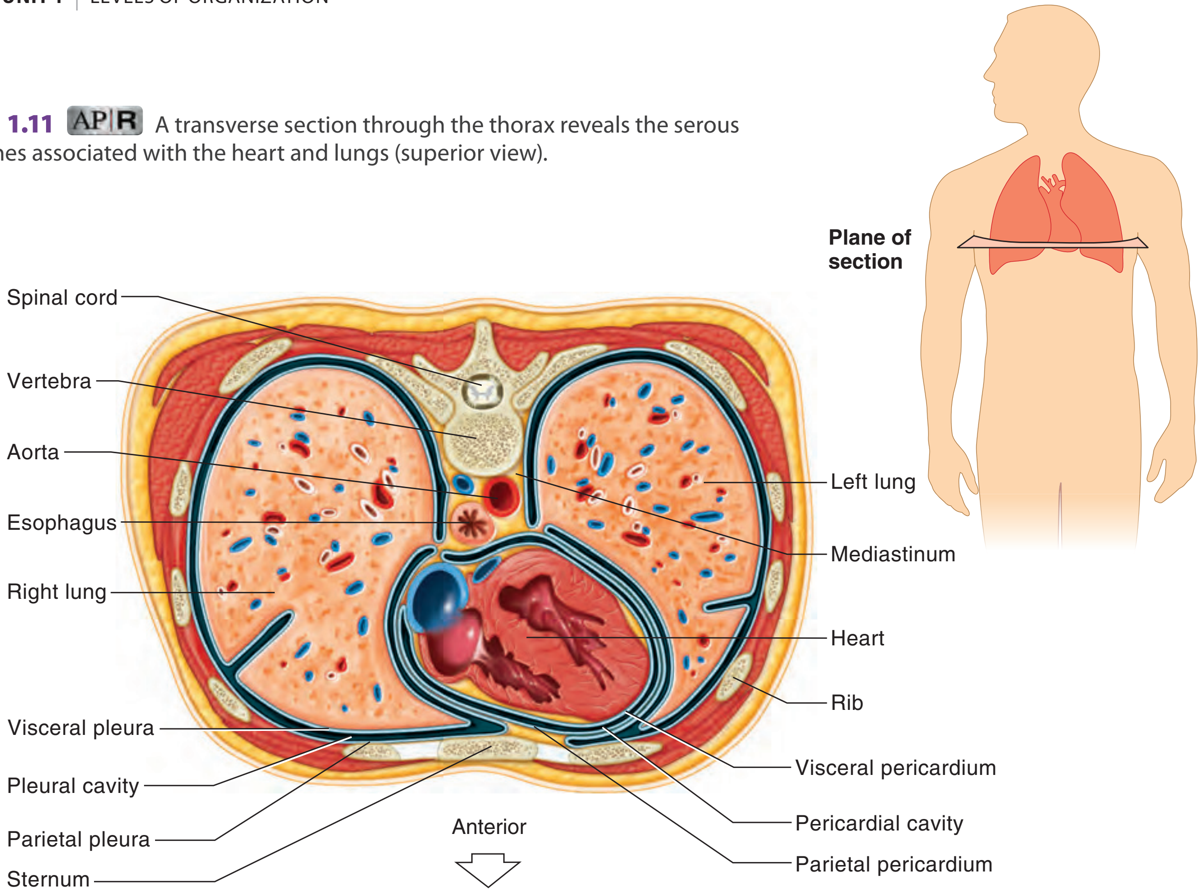
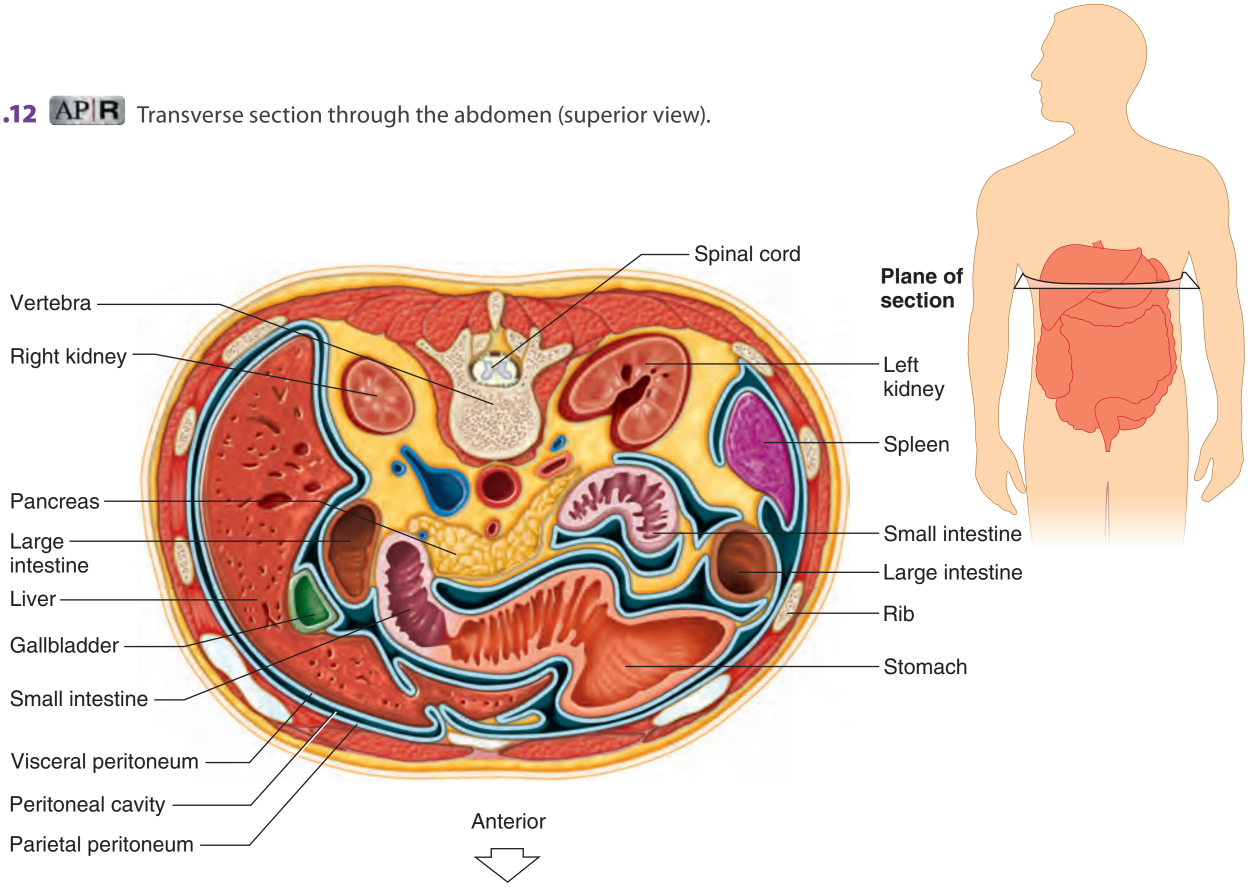

Plane of section
Spinal cord
Vertebra
Aorta
Esophagus
Right lung
Visceral pleura
Pleural cavity
Parietal pleura
Sternum
Left lung
Mediastinum
Heart
Rib
Visceral pericardium
Pericardial cavity
Parietal pericardium
Anterior

**FIGURE 1.12** APR Transverse section through the abdomen (superior view).


Spinal cord
Plane of section
Vertebra
Right kidney
Left kidney
Spleen
Pancreas
Large intestine
Liver
Gallbladder
Small intestine
Visceral peritoneum
Peritoneal cavity
Parietal peritoneum
Small intestine
Large intestine
Rib
Stomach
Anterior

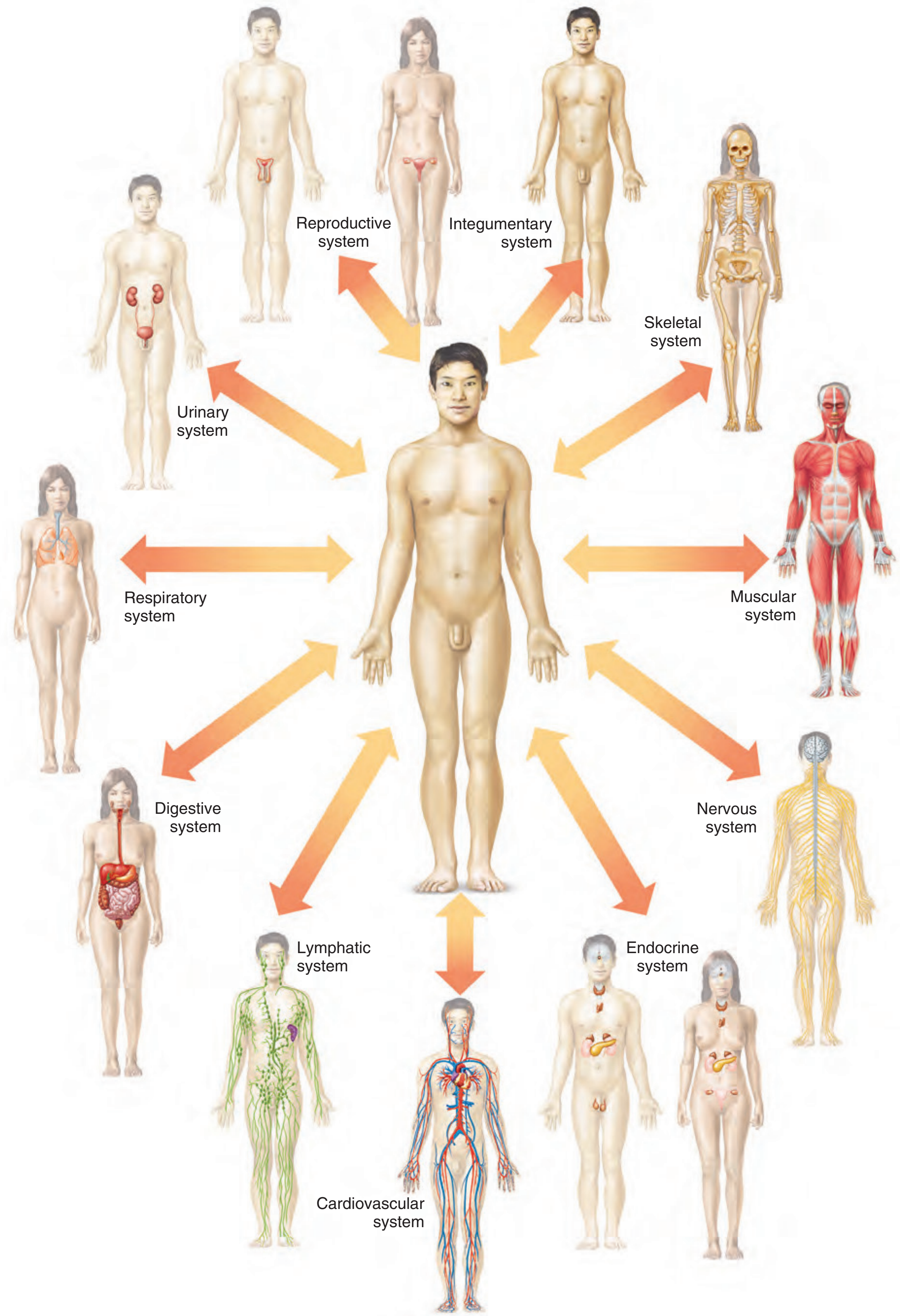

Reproductive system
Integumentary system
Skeletal system
Urinary system
Respiratory system
Muscular system
Digestive system
Nervous system
Lymphatic system
Endocrine system
Cardiovascular system

**FIGURE 1.13** APR The organ systems in humans interact, maintaining homeostasis.

### *Support and Movement*

The organs of the skeletal and muscular systems (see chapters 7 and 8) support and move body parts. The **skeletal** (skel′ĕ-tal) **system** consists of bones, as well as ligaments and cartilages that bind bones together. These parts provide frameworks and protective shields for softer tissues, are attachments for muscles, and act with muscles when body parts move. Tissues within bones also produce blood cells and store inorganic salts.

Muscles are the organs of the **muscular** (mus′ku-lar) **system.** By contracting and pulling their ends closer together, muscles provide forces that move body parts. They also maintain posture and are the major source of body heat.

### *Integration and Coordination*

For the body to act as a unit, its parts must be integrated and coordinated. The nervous and endocrine systems control and adjust various organ functions, thus helping to maintain homeostasis.

The **nervous** (ner′vus) **system** (see chapter 9) consists of the brain, the spinal cord, nerves, and sense organs (see chapter 10). The cells of the nervous system communicate with each other and with muscles and glands using chemical signals called *neurotransmitters.* Each neurotransmitter exerts a relatively short-term effect. Some nerve cells are specialized receptors that detect changes inside and outside the body. Other nerve cells receive information from these receptors and interpret and respond to that information. Still other nerve cells extend from the brain or spinal cord to muscles or glands, stimulating them to contract or to secrete products, respectively.

The **endocrine** (en′do-krin) **system** (see chapter 11) includes all the glands that secrete chemical messengers called *hormones.* The hormones, in turn, move away from the glands in body fluids, such as blood or tissue fluid (fluid from the spaces within tissues). A particular hormone affects only a particular group of cells, called its *target cells.* A hormone alters the metabolism of its target cells. Compared to the action of a neurotransmitter, hormonal effects start less rapidly and last longer. Organs of the endocrine system include the hypothalamus of the brain; the pituitary, thyroid, parathyroid, and adrenal glands; and the pancreas, ovaries, testes, pineal gland, and thymus.

### *Transport*

Two organ systems transport substances throughout the internal environment. The **cardiovascular** (kahr″de-o-vas′ku-lur) **system** (see chapters 12 and 13) includes the heart, arteries, veins, capillaries, and blood. The heart is a muscular pump that helps force blood through the blood vessels. Blood transports gases, nutrients, hormones, and wastes. It carries oxygen from the lungs and nutrients from the digestive organs to all body cells, where these biochemicals are used in metabolic processes. Blood also transports hormones and carries wastes from body cells to the excretory organs, where the wastes are removed from the blood and released to the outside.

The **lymphatic** (lim-fat′ik) **system** (see chapter 14) is closely related to the cardiovascular system. It is composed of the lymphatic vessels, lymph nodes, thymus, spleen, and a fluid called *lymph.* This system transports some of the tissue fluid back to the bloodstream and carries certain fatty substances away from the digestive organs and into the bloodstream. Cells of the lymphatic system are called lymphocytes, and they defend the body against infections by removing disease-causing microorganisms and viruses from tissue fluid.

### *Absorption and Excretion*

Organs in several systems absorb nutrients and oxygen and excrete various wastes. For example, the organs of the **digestive** (di-jest′iv) **system** (see chapter 15) receive foods from the outside. Then they break down food molecules into simpler forms that can pass through cell membranes and thereby be absorbed into the body fluids. Materials that are not absorbed are eliminated. Certain digestive organs also produce hormones and thus function as parts of the endocrine system. The digestive system includes the mouth, tongue, teeth, salivary glands, pharynx, esophagus, stomach, liver, gallbladder, pancreas, small intestine, and large intestine. Chapter 15 also discusses nutrition.

The organs of the **respiratory** (re-spi′rah-to″re) **system** (see chapter 16) move air in and out of the lungs and exchange gases between the blood and the air. Specifically, oxygen passes from air within the lungs into the blood, and carbon dioxide leaves the blood and enters the air. The nasal cavity, pharynx, larynx, trachea, bronchi, and lungs are parts of this system.

The **urinary** (u′rĭ-ner″e) **system** (see chapter 17) consists of the kidneys, ureters, urinary bladder, and urethra. The kidneys remove wastes from blood and help maintain the body's water and electrolyte (salts, acids, and bases) concentrations. The by-product of these activities is urine. Other portions of the urinary system store urine and transport it outside the body. Chapter 18 discusses the urinary system's role in maintaining water and electrolyte concentrations and the acidity of the internal environment.

### *Reproduction*

Reproduction is the process of producing offspring (progeny). Cells reproduce when they divide and give rise to new cells. However, the **reproductive** (re″pro-duk′tiv) **systems** of a male and female work together to produce a new organism (see chapter 19).

The male reproductive system includes the scrotum, testes, epididymides, ductus deferentia, seminal vesicles, prostate gland, bulbourethral glands, penis, and urethra. These parts produce and maintain sperm cells (spermatozoa). Components of the male reproductive system also transfer sperm cells into the female reproductive tract.

The female reproductive system consists of the ovaries, uterine tubes, uterus, vagina, clitoris, and vulva. These organs produce and maintain the female sex cells (egg cells, or oocytes), transport the female sex cells within the female reproductive system, and can receive the male sex cells (sperm cells) for the possibility of fertilizing an egg. The female reproductive system also supports development of embryos, carries fetuses to term, and functions in the birth process.

**PRACTICE**

17. Name and list the organs of the major organ systems.
18. Describe the general functions of each organ system.

## 1.7 | Anatomical Terminology

To communicate effectively with one another, researchers and clinicians have developed a set of precise terms to describe anatomy. These terms concern the relative positions of body parts, relate to imaginary planes along which cuts may be made, and describe body regions.

Use of such terms assumes that the body is in the **anatomical position.** This means that the body is standing erect, face forward, with the upper limbs at the sides and the palms forward. Note that the terms "right" and "left" refer to the right and left of the body in anatomical position.

### Relative Positions

Terms of relative position describe the location of one body part with respect to another. They include the following (many of these terms are illustrated in fig. 1.14):

1. **Superior** means that a body part is above another part. (The thoracic cavity is superior to the abdominopelvic cavity.)
2. **Inferior** means that a body part is below another body part. (The neck is inferior to the head.)
3. **Anterior** (*ventral*) means toward the front. (The eyes are anterior to the brain.)
4. **Posterior** (*dorsal*) means toward the back. (The pharynx is posterior to the oral cavity.)
5. **Medial** refers to an imaginary midline dividing the body into equal right and left halves. A body part is medial if it is closer to midline than another part. (The nose is medial to the eyes.)
6. **Lateral** means toward the side, away from midline. (The ears are lateral to the eyes.)
7. **Bilateral** refers to paired structures, one of which is on each side. (The lungs are bilateral.)
8. **Ipsilateral** refers to structures on the same side. (The right lung and the right kidney are ipsilateral.)
9. **Contralateral** refers to structures on the opposite side. (A patient with a fractured bone in the right leg would have to bear weight on the contralateral—in this case, left—lower limb.)
10. **Proximal** describes a body part that is closer to a point of attachment to the trunk than another body part. (The elbow is proximal to the wrist.) *Proximal* may also refer to another reference point, such as the proximal tubules, which are closer to the filtering structures in the kidney.
11. **Distal** is the opposite of proximal. It means that a particular body part is farther from a point of attachment to the trunk than another body part is. (The fingers are distal to the wrist.) Distal may also refer to another reference point, such as decreased blood flow distal to blockage of a coronary artery.

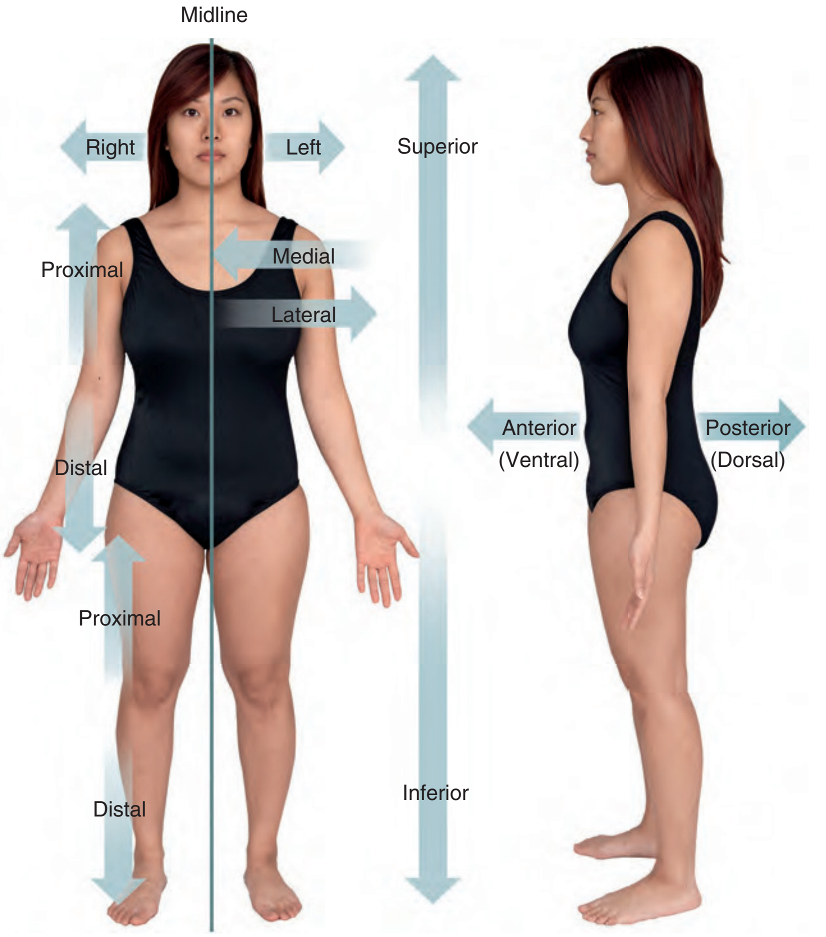


**FIGURE 1.14** APR Relative positional terms describe a body part's location with respect to other body parts.

Q *Which is more lateral, the hand or the hip?*
**Answer can be found in Appendix F on page 582.**

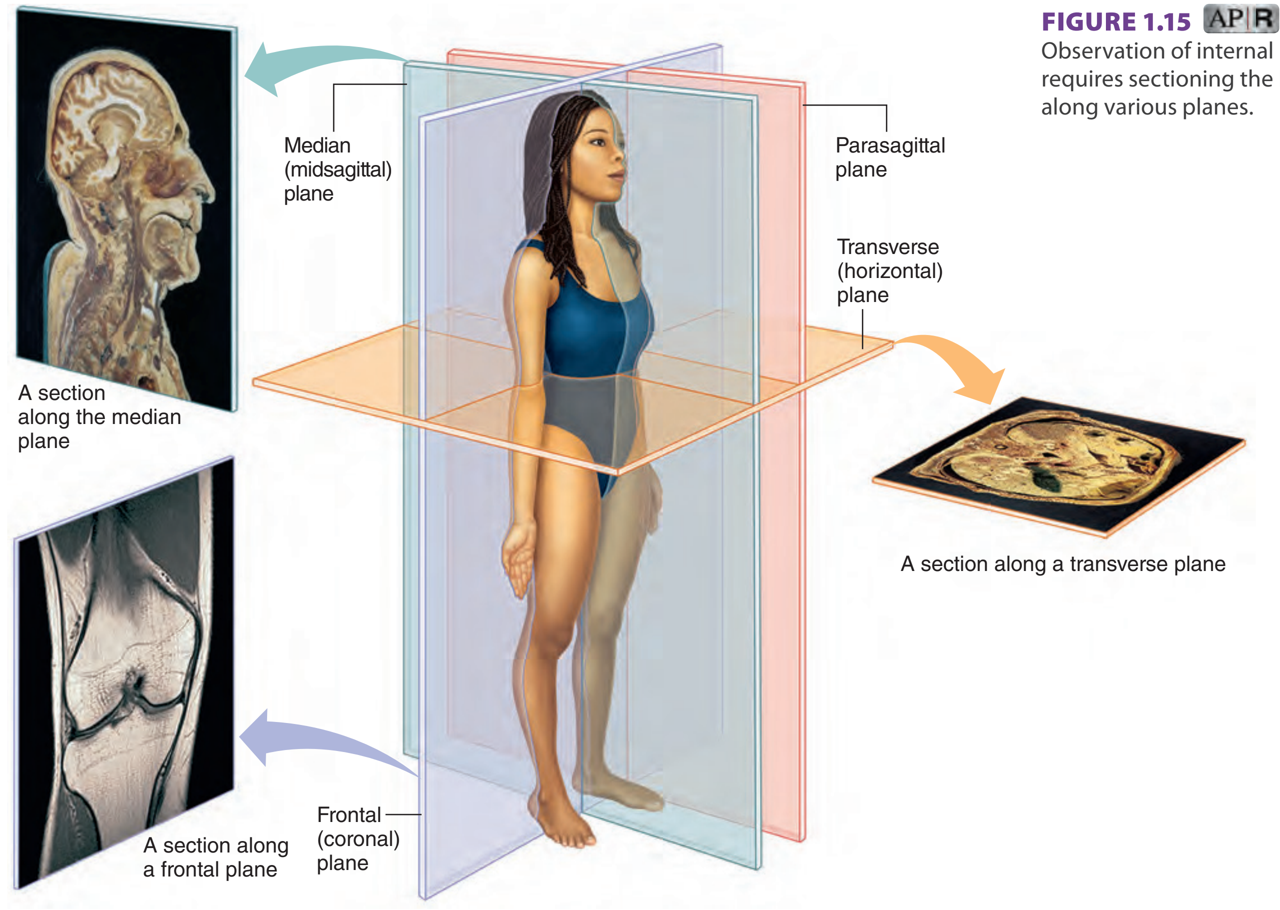

Median
(midsagittal)
plane
Parasagittal
plane
Transverse
(horizontal)
plane
A section
along the median
plane
A section along a transverse plane
A section along
a frontal plane
Frontal
(coronal)
plane

**FIGURE 1.15** APR Observation of internal parts requires sectioning the body along various planes.

12. **Superficial** means situated near the surface. (The epidermis is the superficial layer of the skin.) *Peripheral* also means outward or near the surface. It describes the location of certain blood vessels and nerves. (The nerves that branch from the brain and spinal cord are peripheral nerves.)
13. **Deep** describes parts that are more internal than superficial parts. (The dermis is the deep layer of the skin.)

## Body Sections

Observing the relative locations and organization of internal body parts requires cutting or sectioning the body along various planes (fig. 1.15). The following terms describe such planes and the sections that result:

1. **Sagittal** refers to a lengthwise plane that divides the body into right and left portions. If a sagittal plane passes along the midline and thus divides the body into equal parts, it is called *median* (midsagittal). A sagittal section lateral to midline is called *parasagittal.*
2. **Transverse** (*horizontal*) refers to a plane that divides the body into superior and inferior portions.
3. **Frontal** (*coronal*) refers to a plane that divides the body into anterior and posterior portions.

Sometimes, a cylindrical organ such as a long bone is sectioned. In this case, a cut across the structure is called a *cross section,* an angular cut is an *oblique section,* and a lengthwise cut is a *longitudinal section* (fig. 1.16). Clinical Application 1.1 discusses using computerized tomography to view body sections.

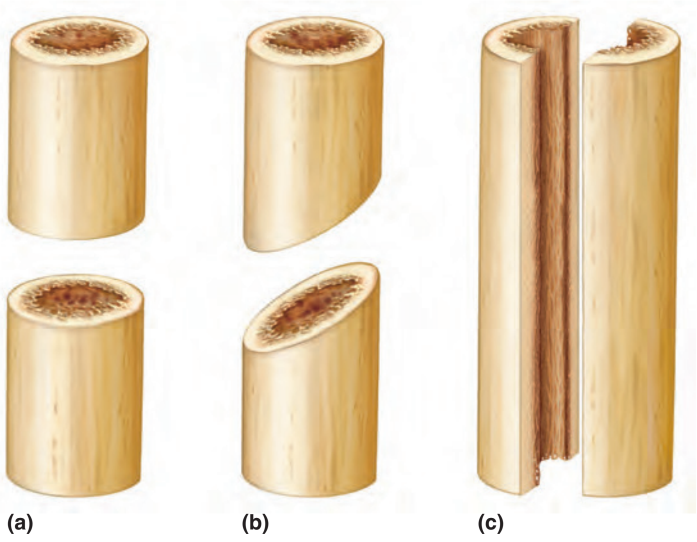


**FIGURE 1.16** Cylindrical parts may be cut in **(a)** cross section, **(b)** oblique section, or **(c)** longitudinal section.

### CLINICAL APPLICATION 1.1

## Computerized Tomography

Radiologists use a procedure called *computerized tomography,* or CT scanning, to visualize internal organ sections (fig. 1A). In this procedure, an X-ray-emitting device moves around the body region being examined or it may image the entire body. At the same time, an X-ray detector moves in the opposite direction on the other side. As the devices move, an X-ray beam passes through the body from hundreds of different angles. Because tissues and organs of varying composition within the body absorb X rays differently, the amount of X ray reaching the detector varies from position to position. A computer records the measurements from the X-ray detector, and combines them mathematically to create a sectional image of the internal body parts that can be viewed on a monitor.

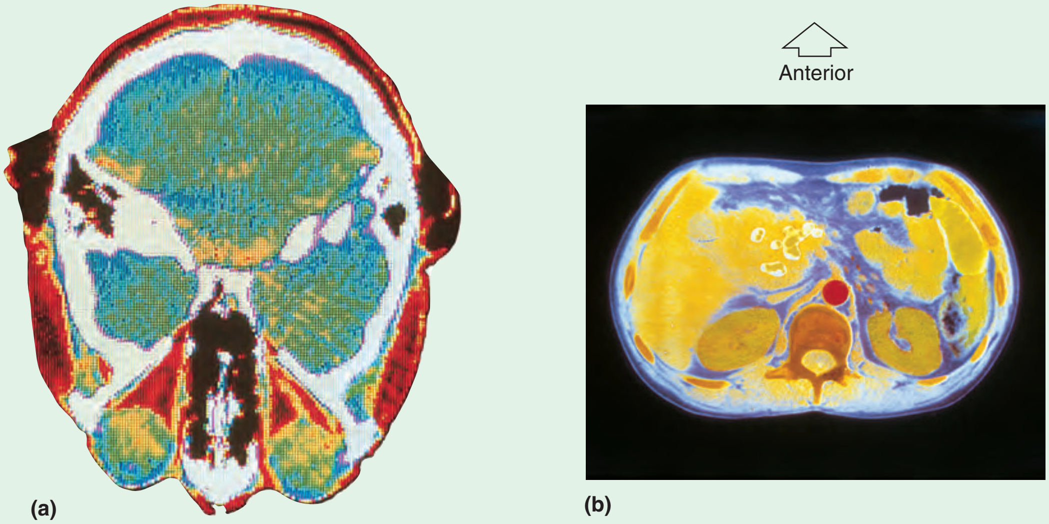


**FIGURE 1A** Falsely colored CT (computerized tomography) scans of **(a)** the head and **(b)** the abdomen. *Note:* These are not shown in correct relative size.

## Body Regions

A number of terms designate body regions. The abdominal area, for example, is subdivided into the following nine regions, as figure 1.17*a* shows:

1. The **epigastric region** is the upper middle portion.
2. The **right** and **left hypochondriac regions** lie on each side of the epigastric region.
3. The **umbilical region** is the middle portion.
4. The **right** and **left lateral (lumbar) regions** lie on each side of the umbilical region.
5. The **pubic (hypogastric) region** is the lower middle portion.
6. The **right** and **left inguinal (iliac) regions** lie on each side of the hypogastric region.

The abdominal area is also often subdivided into four quadrants, as figure 1.17*b* shows.

The following adjectives are commonly used to refer to various body regions, some of which are illustrated in figure 1.18:

**abdominal** (ab-dom′ĭ-nal) The region between the thorax and pelvis.
**acromial** (ah-kro′me-al) The point of the shoulder.
**antebrachial** (an″te-bra′ke-al) The forearm.
**antecubital** (an″te-ku′bĭ-tal) The space in front of the elbow.
**axillary** (ak′sĭ-ler″e) The armpit.
**brachial** (bra′ke-al) The arm.
**buccal** (buk′al) The cheek.
**calcaneal** (cal-ca-ne-al) The heel.
**carpal** (kar′pal) The wrist.
**celiac** (se′le-ak) The abdomen.
**cephalic** (sĕ-fal′ik) The head.
**cervical** (ser′vĭ-kal) The neck.
**costal** (kos′tal) The ribs.
**coxal** (kok′sal) The hip.
**crural** (kroor′al) The leg.
**cubital** (ku′bĭ-tal) The elbow.
**digital** (dij′ĭ-tal) The finger or toe.
**dorsal** (dor′sal) The back.
**femoral** (fem′or-al) The thigh.

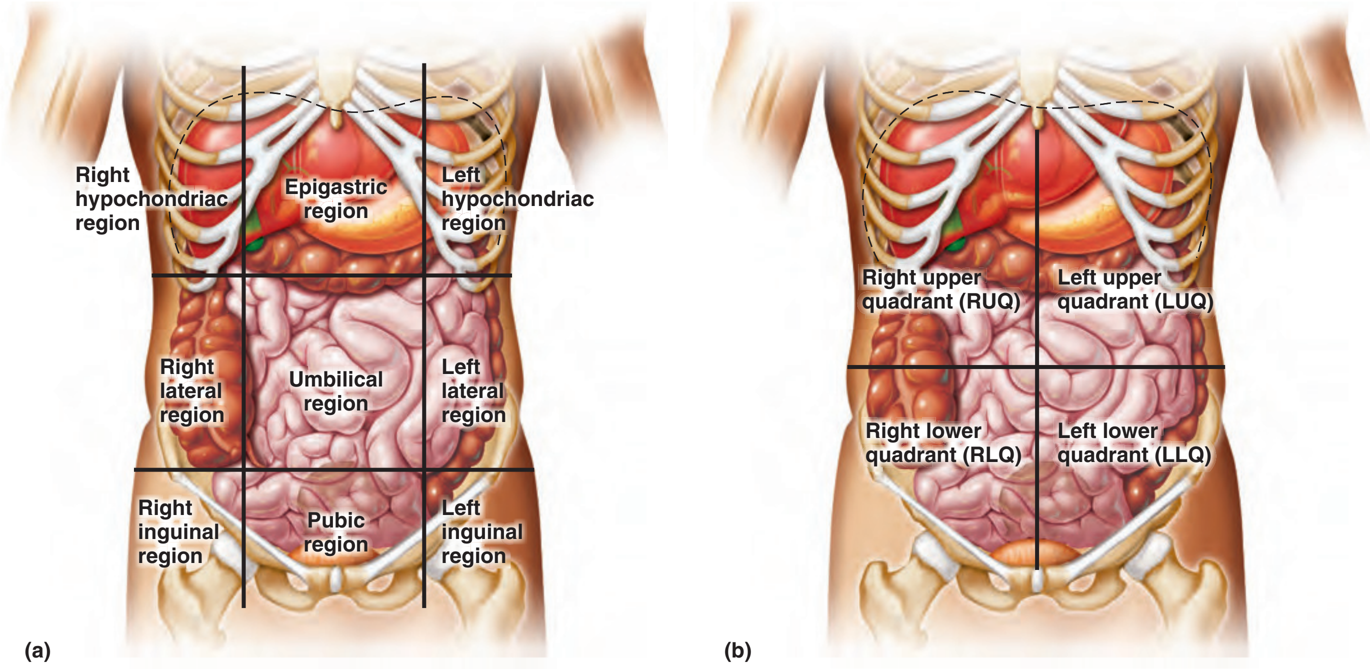

Right hypochondriac region
Epigastric region
Left hypochondriac region
Right lateral region
Umbilical region
Left lateral region
Right inguinal region
Pubic region
Left inguinal region
(a)
Right upper quadrant (RUQ)
Left upper quadrant (LUQ)
Right lower quadrant (RLQ)
Left lower quadrant (LLQ)
(b)

**FIGURE 1.17** APR The abdominal area is commonly subdivided in two ways: **(a)** into nine regions and **(b)** into four quadrants.

**frontal** (frun′tal) The forehead.
**genital** (jen′ĭ-tal) The reproductive organs.
**gluteal** (gloo′te-al) The buttocks.
**inguinal** (ing′gwĭ-nal) The groin—the depressed area of the abdominal wall near the thigh.
**lumbar** (lum′bar) The loin—the region of the lower back between the ribs and the pelvis.
**mammary** (mam′er-e) The breast.
**mental** (men′tal) The chin.
**nasal** (na′zal) The nose.
**occipital** (ok-sip′ĭ-tal) The lower posterior region of the head.
**oral** (o′ral) The mouth.
**orbital** (or′bi-tal) The bony socket of the eye.
**palmar** (pahl′mar) The palm of the hand.
**patellar** (pah-tel′ar) The front of the knee.
**pectoral** (pek′tor-al) The chest.
**pedal** (ped′al) The foot.
**pelvic** (pel′vik) The pelvis.
**perineal** (per″ĭ-ne′al) The perineum—the pelvic floor and associated structures occupying the pelvic outlet.
**plantar** (plan′tar) The sole of the foot.
**popliteal** (pop″lĭ-te′al) The area behind the knee.
**sacral** (sa′kral) The posterior region between the hip bones.
**sternal** (ster′nal) The middle of the thorax, anteriorly.
**sural** (su′ral) The calf of the leg.
**tarsal** (tahr′sal) The ankle.
**umbilical** (um-bil′ĭ-kal) The navel.
**vertebral** (ver′te-bral) The spinal column.

## PRACTICE

19. Describe the anatomical position.
20. Using the appropriate terms, describe the relative positions of several body parts.
21. Describe the three types of body sections.
22. Name the nine regions of the abdomen.

## SOME MEDICAL AND APPLIED SCIENCES

**cardiology** (kar″de-ol′o-je) Branch of medical science dealing with the heart and heart diseases.
**cytology** (si-tol′o-je) Study of the structure, function, and abnormalities of cells. Cytology and histology are subdivisions of microscopic anatomy.
**dermatology** (der″mah-tol′o-je) Study of the skin and its diseases.
**endocrinology** (en″do-krĭ-nol′o-je) Study of hormones, hormone-secreting glands, and their diseases.
**epidemiology** (ep″ĭ-de″me-ol′o-je) Study of the factors determining the distribution and frequency of health-related conditions in a defined human population.
**gastroenterology** (gas″tro-en″ter-ol′o-je) Study of the stomach and intestines and their diseases.
**geriatrics** (jer″e-at′riks) Branch of medicine dealing with older individuals and their medical problems.

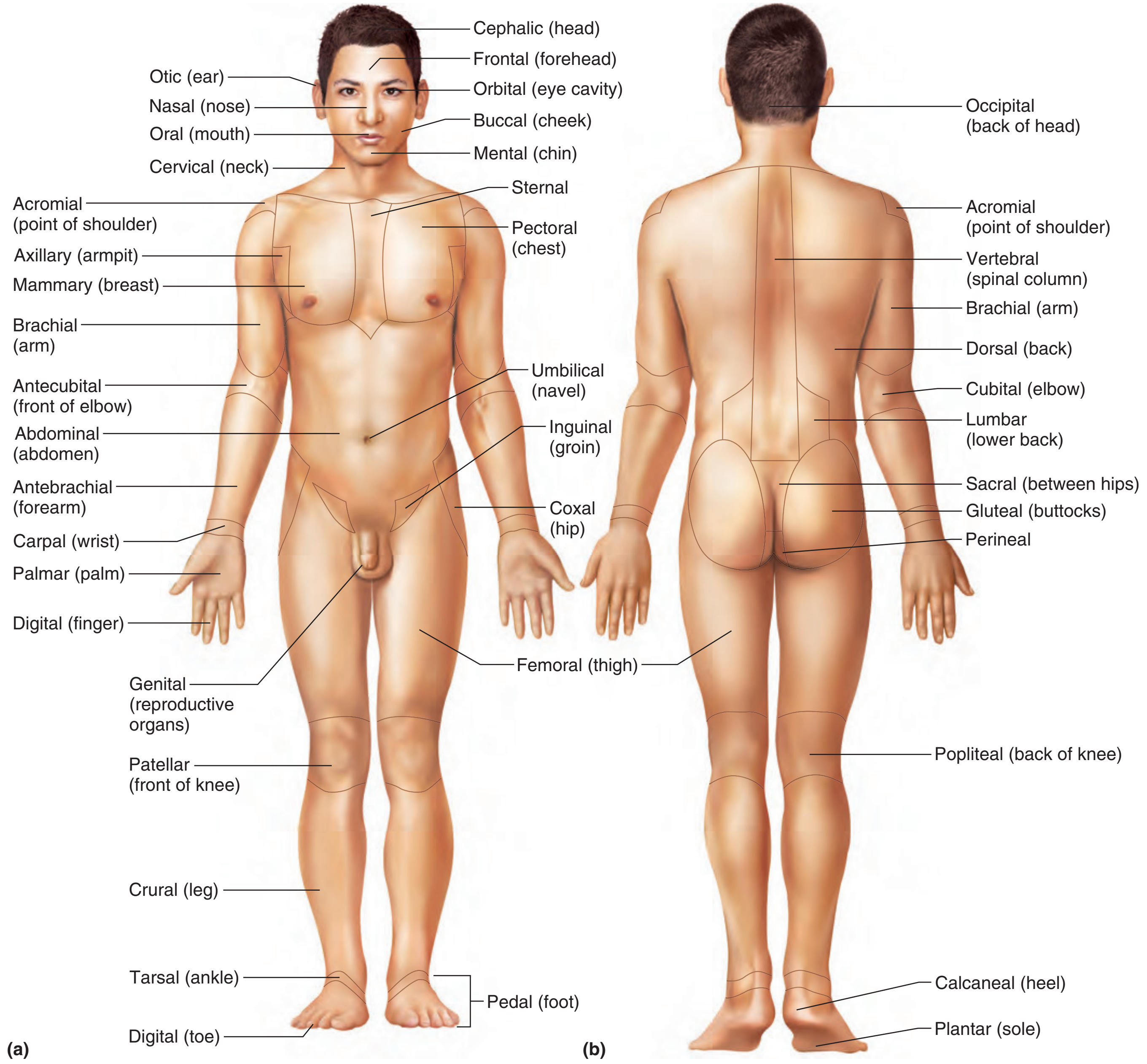

Otic (ear)
Nasal (nose)
Oral (mouth)
Cervical (neck)
Cephalic (head)
Frontal (forehead)
Orbital (eye cavity)
Buccal (cheek)
Mental (chin)
Sternal
Acromial (point of shoulder)
Pectoral (chest)
Axillary (armpit)
Mammary (breast)
Brachial (arm)
Umbilical (navel)
Antecubital (front of elbow)
Inguinal (groin)
Abdominal (abdomen)
Antebrachial (forearm)
Coxal (hip)
Carpal (wrist)
Palmar (palm)
Digital (finger)
Femoral (thigh)
Genital (reproductive organs)
Patellar (front of knee)
Crural (leg)
Tarsal (ankle)
Pedal (foot)
Digital (toe)
(a)
(b)
Occipital (back of head)
Acromial (point of shoulder)
Vertebral (spinal column)
Brachial (arm)
Dorsal (back)
Cubital (elbow)
Lumbar (lower back)
Sacral (between hips)
Gluteal (buttocks)
Perineal
Popliteal (back of knee)
Calcaneal (heel)
Plantar (sole)

**FIGURE 1.18** APR Some terms used to describe body regions. **(a)** Anterior regions. **(b)** Posterior regions.

**gerontology** (jer″on-tol′o-je) Study of the aging process.

**gynecology** (gi″nĕ-kol′o-je) Study of the female reproductive system and its diseases.

**hematology** (hēm″ah-tol′o-je) Study of the blood and blood diseases.

**histology** (his-tol′o-je) Study of the structure and function of tissues. Histology and cytology are subdivisions of microscopic anatomy.

**immunology** (im″u-nol′o-je) Study of the body's resistance to infectious disease.

**neonatology** (ne″o-na-tol′o-je) Study of newborns and the treatment of their disorders.

**nephrology** (nĕ-frol′o-je) Study of the structure, function, and diseases of the kidneys.

**neurology** (nu-rol′o-je) Study of the nervous system and its disorders.

**obstetrics** (ob-stet′riks) Branch of medicine dealing with pregnancy and childbirth.

**oncology** (ong-kol′o-je) Study of cancers.

**ophthalmology** (of″thal-mol′o-je) Study of the eye and eye diseases.

**orthopedics** (or″tho-pe′diks) Branch of medicine dealing with the muscular and skeletal systems and their problems.

**otolaryngology** (o″to-lar″in-gol′o-je) Study of the ear, throat, and larynx, and their diseases.

**pathology** (pah-thol′o-je) Study of structural and functional changes that disease causes.

**pediatrics** (pe″de-at′riks) Branch of medicine dealing with children and their diseases.

**pharmacology** (fahr″mah-kol′o-je) Study of drugs and their uses in the treatment of disease.

**podiatry** (po-di′ah-tre) Study of the care and treatment of feet.

**psychiatry** (si-ki′ah-tre) Branch of medicine dealing with the mind and its disorders.

**radiology** (ra″de-ol′o-je) Study of X rays and radioactive substances and their uses in the diagnosis and treatment of diseases.

**toxicology** (tok″sĭ-kol′o-je) Study of poisonous substances and their effects upon body parts.

**urology** (u-rol′o-je) Branch of medicine dealing with the urinary system, apart from the kidneys (nephrology) and the male reproductive system, and their diseases.

## Summary Outline

### 1.1 Introduction (p. 10)

1. Early interest in the human body probably developed as people became concerned about injuries and illnesses.
2. Primitive doctors began to learn how certain herbs and potions affected body functions.
3. The belief that humans could understand forces that caused natural events led to the development of modern science.
4. A set of terms originating from Greek and Latin words is the basis for the language of anatomy and physiology.
5. Used to investigate the human body, the scientific method tests a hypothesis, then rejects or accepts it based on the results of experiments or observations.

### 1.2 Anatomy and Physiology (p. 11)

1. Anatomy describes the form and organization of body parts.
2. Physiology considers the functions of anatomical parts.
3. The function of a body part depends on the way it is constructed.

### 1.3 Levels of Organization (p. 12)

*The body is composed of parts with different levels of complexity.*

1. Matter is composed of atoms.
2. Atoms join to form molecules.
3. Organelles are built of groups of large molecules (macromolecules).
4. Cells, which contain organelles, are the basic units of structure and function that form the body.
5. Cells are organized into tissues.
6. Tissues are organized into organs.
7. Organs that function closely together compose organ systems.
8. Organ systems constitute the organism.
9. Beginning at the atomic level, these levels of organization differ in complexity from one level to the next.

### 1.4 Characteristics of Life (p. 13)

*Characteristics of life are traits all organisms share.*

1. These characteristics include:
   a. Movement—changing body position or moving internal parts.
   b. Responsiveness—sensing and reacting to internal or external changes.
   c. Growth—increasing size without changing shape.
   d. Reproduction—producing offspring.
   e. Respiration—obtaining oxygen, using oxygen to release energy from foods, and removing gaseous wastes.
   f. Digestion—breaking down food substances into component nutrients that the intestine can absorb.
   g. Absorption—moving substances through membranes and into body fluids.
   h. Circulation—moving substances through the body in body fluids.
   i. Assimilation—changing substances into chemically different forms.
   j. Excretion—removing body wastes.
2. Acquisition and use of energy constitute metabolism.

### 1.5 Maintenance of Life (p. 13)

*The structures and functions of body parts maintain the life of the organism.*

1. Requirements of organisms
   a. Water is used in many metabolic processes, provides the environment for metabolic reactions, and transports substances.
   b. Food supplies energy, raw materials for building new living matter, and chemicals necessary in vital reactions.
   c. Oxygen releases energy from food materials. This energy drives metabolic reactions.
   d. Heat is a product of metabolic reactions and helps govern the rates of these reactions.
   e. Pressure is an application of force to something. In humans, atmospheric and hydrostatic pressures help breathing and blood movements, respectively.
2. Homeostasis
   a. If an organism is to survive, the conditions within its body fluids must remain relatively stable.
   b. Maintenance of a stable internal environment is called *homeostasis*.
   c. Homeostatic mechanisms help regulate body temperature and blood pressure.
   d. Homeostatic mechanisms act through negative feedback.

### 1.6 Organization of the Human Body (p. 16)

1. Body cavities
   a. The axial portion of the body includes the cranial cavity, the vertebral canal, the thoracic cavity, and the abdominopelvic cavity.
   b. The diaphragm separates the thoracic and abdominopelvic cavities.
   c. The organs in a body cavity are called *viscera*.
   d. The mediastinum separates the thoracic cavity into right and left compartments.
   e. Body cavities in the head include the oral, nasal, orbital, and middle ear cavities.
2. Thoracic and abdominopelvic membranes
   a. Thoracic membranes
      (1) Pleural membranes line the thoracic cavity (parietal pleura) and cover each lung (visceral pleura).
      (2) Pericardial membranes surround the heart (parietal pericardium) and cover its surface (visceral pericardium).
      (3) The pleural and pericardial cavities are the potential spaces between the respective parietal and visceral membranes.
   b. Abdominopelvic membranes
      (1) Peritoneal membranes line the abdominopelvic cavity (parietal peritoneum) and cover the organs inside (visceral peritoneum).
      (2) The peritoneal cavity is the potential space between the parietal and visceral membranes.

3. Organ systems
   *The human organism consists of several organ systems. Each system includes a set of interrelated organs.*
   a. Body covering
      (1) The integumentary system includes the skin, hair, nails, sweat glands, and sebaceous glands.
      (2) It protects underlying tissues, regulates body temperature, houses sensory receptors, and synthesizes various substances.
   b. Support and movement
      (1) Skeletal system
         (a) The skeletal system is composed of bones, as well as cartilages and ligaments that bind bones together.
         (b) It provides a framework, protective shields, and attachments for muscles. It also produces blood cells and stores inorganic salts.
      (2) Muscular system
         (a) The muscular system includes the muscles of the body.
         (b) It moves body parts, maintains posture, and produces body heat.
   c. Integration and coordination
      (1) Nervous system
         (a) The nervous system consists of the brain, spinal cord, nerves, and sense organs.
         (b) It receives information from sensory receptors, interprets the information, and stimulates muscles or glands to respond.
      (2) Endocrine system
         (a) The endocrine system consists of glands that secrete hormones.
         (b) Hormones help regulate metabolism.
         (c) This system includes the hypothalamus of the brain and the pituitary, thyroid, parathyroid, and adrenal glands, as well as the pancreas, ovaries, testes, pineal gland, and thymus.
   d. Transport
      (1) Cardiovascular system
         (a) The cardiovascular system includes the heart, which pumps blood, and the blood vessels, which carry blood to and from body parts.
         (b) Blood transports oxygen, nutrients, hormones, and wastes.
      (2) Lymphatic system
         (a) The lymphatic system is composed of lymphatic vessels, lymph fluid, lymph nodes, thymus, and spleen.
         (b) It transports lymph fluid from tissues to the bloodstream, carries certain fatty substances away from the digestive organs, and aids in defending the body against disease-causing agents.
   e. Absorption and excretion
      (1) Digestive system
         (a) The digestive system receives foods, breaks down food molecules into nutrients that can pass through cell membranes, and eliminates materials that are not absorbed.
         (b) It includes the mouth, tongue, teeth, salivary glands, pharynx, esophagus, stomach, liver, gallbladder, pancreas, small intestine, and large intestine.
         (c) Some digestive organs produce hormones.
      (2) Respiratory system
         (a) The respiratory system takes in and sends out air and exchanges gases between the air and blood.
         (b) It includes the nasal cavity, pharynx, larynx, trachea, bronchi, and lungs.
      (3) Urinary system
         (a) The urinary system includes the kidneys, ureters, urinary bladder, and urethra.
         (b) It filters wastes from the blood and helps maintain water and electrolyte concentrations and the acidity of the internal environment.
   f. Reproduction
      (1) The reproductive systems produce new organisms.
      (2) The male reproductive system includes the scrotum, testes, epididymides, ductus deferentia, seminal vesicles, prostate gland, bulbourethral glands, urethra, and penis, which produce, maintain, and transport male sex cells (sperm cells).
      (3) The female reproductive system includes the ovaries, uterine tubes, uterus, vagina, clitoris, and vulva, which produce, maintain, and transport female sex cells (oocytes).

### 1.7 Anatomical Terminology (p. 23)

*Terms with precise meanings help investigators communicate effectively.*

1. Relative positions
   These terms describe the location of one part with respect to another part.
2. Body sections
   Body sections are planes along which the body may be cut to observe the relative locations and organization of internal parts.
3. Body regions
   Special terms designate various body regions.

## CHAPTER ASSESSMENTS

### 1.1 Introduction

**1.** Briefly describe the early discoveries that led to our understanding of the human body. (p. 10)

### 1.2 Anatomy and Physiology

**2.** Explain the difference between anatomy and physiology. (p. 11)
**3.** Identify relationships between the form and the function of body parts. (p. 11)

### 1.3 Levels of Organization

**4.** List the levels of organization within the human body and describe the characteristics of each. (p. 12)

### 1.4 Characteristics of Life

**5.** List and describe ten characteristics of life. (p. 13)
**6.** Define metabolism and give examples. (p. 13)

### 1.5 Maintenance of Life

**7.** List and describe five requirements of organisms. (pp. 13–14)
**8.** Define *homeostasis,* and explain its importance. (p. 14)
**9.** Identify the parts of a homeostatic mechanism and explain how they work together. (p. 14)
**10.** Explain the control of body temperature. (p. 15)
**11.** Describe a homeostatic mechanism that helps regulate blood pressure. (p. 15)

### 1.6 Organization of the Human Body

**12.** Explain the difference between the axial and appendicular portions of the body. (p. 16)
**13.** Identify the cavities within the axial portion of the body. (p. 16)
**14.** Define *viscera*. (p. 16)

**15.** Describe the mediastinum and its contents. (p. 17)

**16.** List the cavities of the head and the contents of each cavity. (p. 17)

**17.** Name the body cavity that houses each of the following organs: (p. 17)

a. Stomach
b. Heart
c. Brain
d. Liver
e. Trachea
f. Rectum
g. Spinal cord
h. Esophagus
i. Spleen
j. Urinary bladder

**18.** Distinguish between a parietal and a visceral membrane. (p. 17)

**19.** Name the major organ systems, and describe the general functions of each. (pp. 19, 21–23)

**20.** List the major organs that compose each organ system. (pp. 19, 21–23)

### 1.7 Anatomical Terminology

**21.** Write complete sentences using each of the following terms to correctly describe the relative positions of specific body parts: (pp. 23–24)

a. Superior
b. Inferior
c. Anterior
d. Posterior
e. Medial
f. Lateral
g. Proximal
h. Distal
i. Superficial
j. Peripheral
k. Deep

**22.** Sketch the outline of a human body, and use lines to indicate an example of each of the following sections: (p. 24)

a. Sagittal
b. Transverse
c. Frontal

**23.** Sketch the abdominal area, and indicate the locations of the following regions: (p. 25)

a. Epigastric
b. Umbilical
c. Pubic
d. Hypochondriac
e. Lateral
f. Inguinal

**24.** Provide the common name for the region to which each of the following terms refers: (pp. 25–26)

a. Acromial
b. Antebrachial
c. Axillary
d. Buccal
e. Celiac
f. Coxal
g. Crural
h. Femoral
i. Genital
j. Gluteal
k. Inguinal
l. Mental
m. Occipital
n. Orbital
o. Otic
p. Palmar
q. Pectoral
r. Pedal
s. Plantar
t. Popliteal
u. Sacral
v. Tarsal
w. Umbilical
x. Vertebral

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 1.2, 1.3, 1.4, 1.5

**1.** Which characteristics of life does a computer have? Why is a computer not alive?

### OUTCOMES 1.2, 1.3, 1.4, 1.5, 1.6

**2.** Put the following in order, from smallest and simplest to largest and most complex, and describe their individual roles in homeostasis: organ, molecule, organelle, atom, organ system, tissue, organism, cell, macromolecule.

### OUTCOMES 1.4, 1.5

**3.** What environmental characteristics would be necessary for a human to survive on another planet?

### OUTCOMES 1.5, 1.6

**4.** In health, body parts interact to maintain homeostasis. Illness can threaten the maintenance of homeostasis, requiring treatment. What treatments might be used to help control a patient's (*a*) body temperature, (*b*) blood oxygen concentration, and (*c*) water content?

### OUTCOMES 1.5, 1.6, 1.7

**5.** How might health-care professionals provide the basic requirements of life to an unconscious patient? Describe the body parts involved in the treatment, using correct directional and regional terms.

### OUTCOME 1.6

**6.** Suppose two individuals develop benign (noncancerous) tumors that produce symptoms because they occupy space and crowd adjacent organs. If one of these persons has the tumor in the thoracic cavity and the other has the tumor in the abdominopelvic cavity, which person would be likely to develop symptoms first? Why? Which might be more immediately serious? Why?

### OUTCOMES 1.6, 1.7

**7.** If a patient complained of a "stomachache" and pointed to the umbilical region as the site of discomfort, which organs located in this region might be the source of the pain?

## ONLINE STUDY TOOLS www.mhhe.com/shieress12

LEARN PRACTICE ASSESS

**Connect Interactive Questions** Reinforce your knowledge using assigned interactive questions covering levels of organization, anatomical terminology, homeostasis, body organization, and more.

**Connect Integrated Activity** Can you help a surgeon localize different sites for incisions?

**LearnSmart** Discover which chapter concepts you have mastered and which require more attention. This adaptive learning tool is personalized, proven, and preferred.

**Anatomy & Physiology Revealed** Go more in depth into the human body by exploring body regions, planes of sections, and organ systems.

REFERENCE PLATES

# THE HUMAN ORGANISM

The series of illustrations that follows shows the major parts of the human torso. The first plate illustrates the anterior surface and reveals the superficial muscles on one side. Each subsequent plate exposes deeper organs, including those in the thoracic, abdominal, and pelvic cavities.

Chapters 6–19 of this textbook describe the organs and organ systems of the human organism in detail. As you read them, refer to these plates to visualize the locations of various organs and the three-dimensional relationships among them.

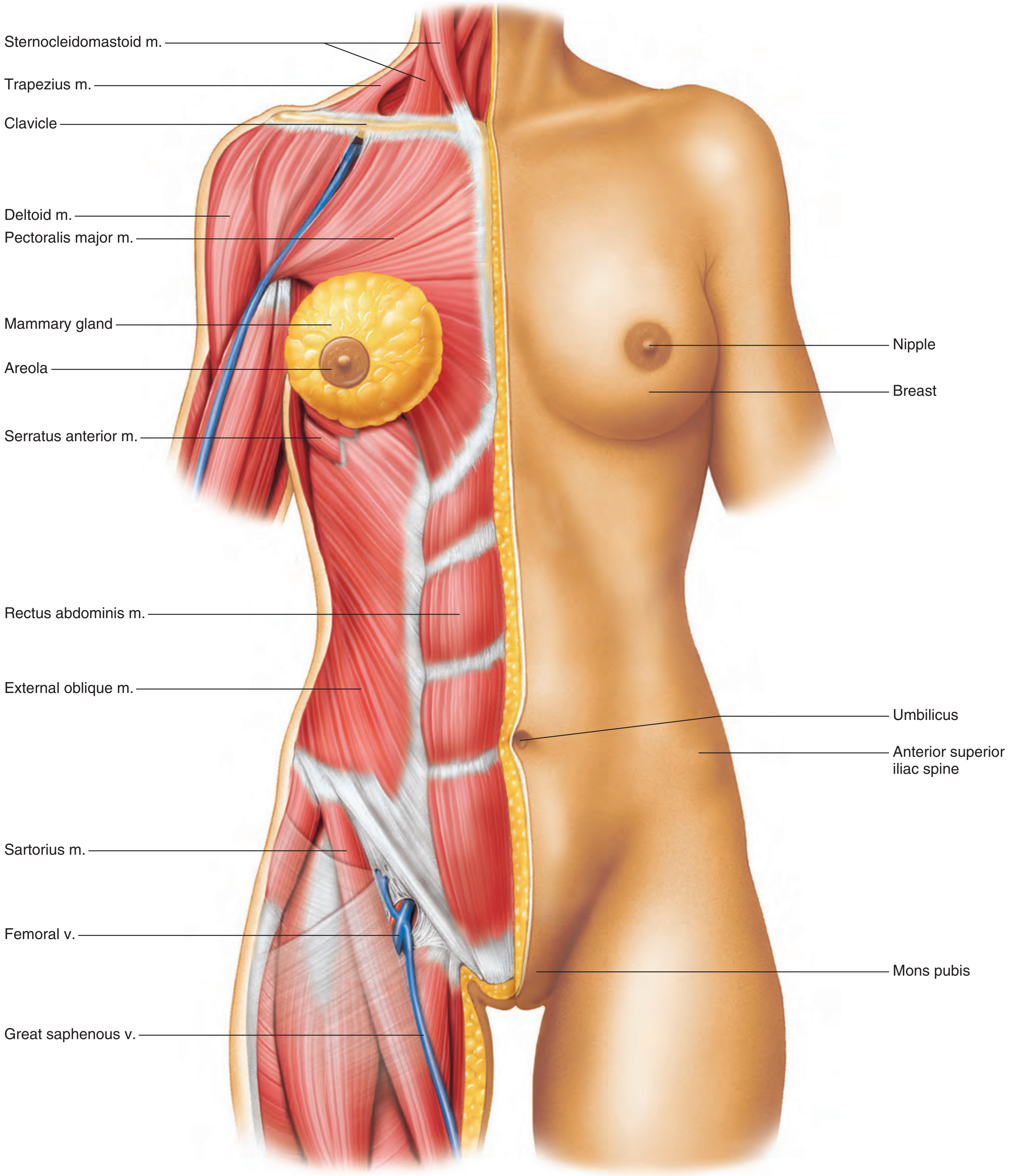

Sternocleidomastoid m.
Trapezius m.
Clavicle
Deltoid m.
Pectoralis major m.
Mammary gland
Areola
Serratus anterior m.
Rectus abdominis m.
External oblique m.
Sartorius m.
Femoral v.
Great saphenous v.
Nipple
Breast
Umbilicus
Anterior superior iliac spine
Mons pubis

**PLATE ONE** Human female torso showing the anterior surface on one side and the superficial muscles exposed on the other side. (*m.* stands for *muscle,* and *v.* stands for *vein.*)

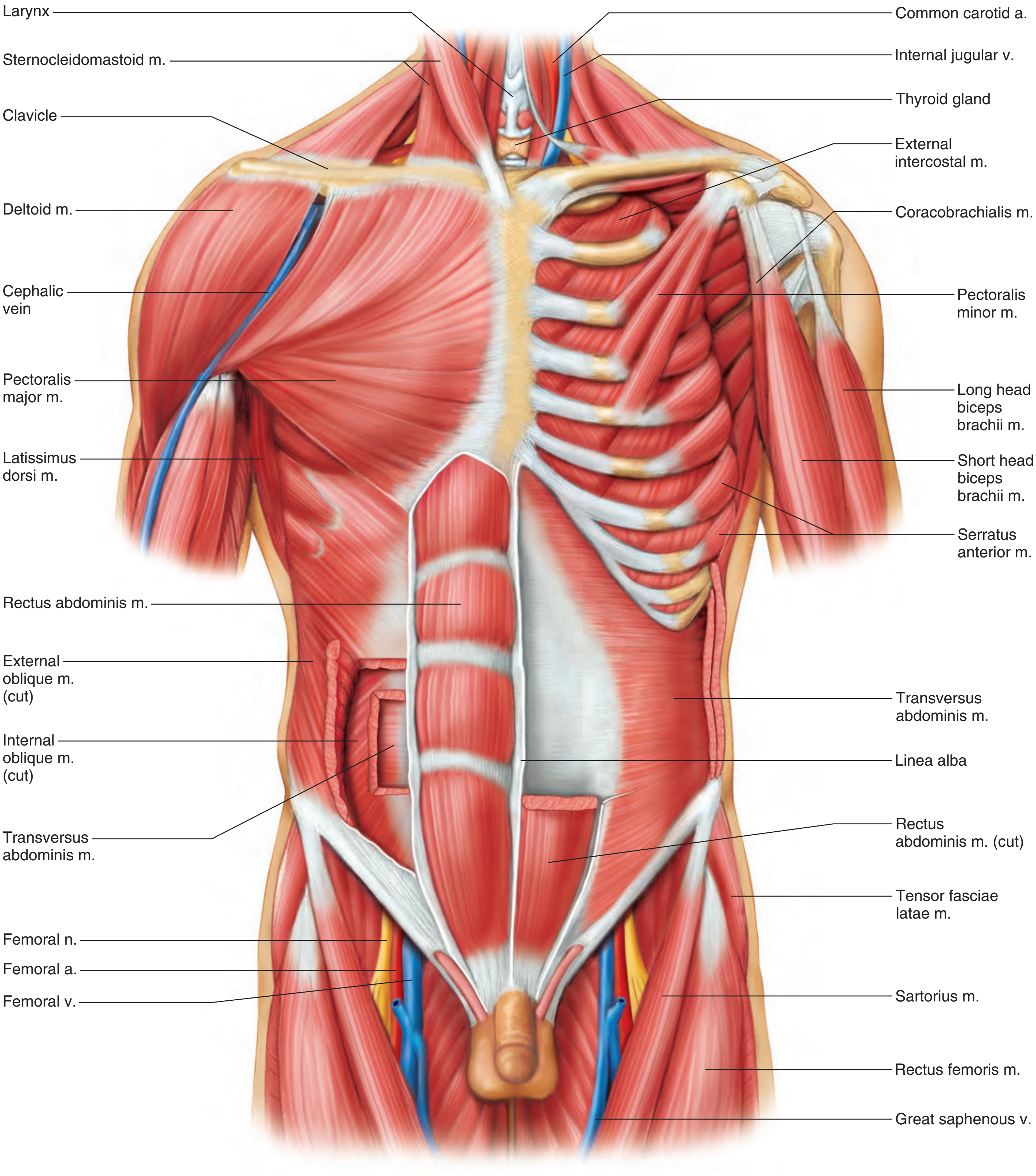

Larynx
Sternocleidomastoid m.
Clavicle
Deltoid m.
Cephalic vein
Pectoralis major m.
Latissimus dorsi m.
Rectus abdominis m.
External oblique m. (cut)
Internal oblique m. (cut)
Transversus abdominis m.
Femoral n.
Femoral a.
Femoral v.
Common carotid a.
Internal jugular v.
Thyroid gland
External intercostal m.
Coracobrachialis m.
Pectoralis minor m.
Long head biceps brachii m.
Short head biceps brachii m.
Serratus anterior m.
Transversus abdominis m.
Linea alba
Rectus abdominis m. (cut)
Tensor fasciae latae m.
Sartorius m.
Rectus femoris m.
Great saphenous v.

**PLATE TWO** Human male torso with the deeper muscle layers exposed.
(*n.* stands for *nerve, a.* stands for *artery, m.* stands for *muscle,* and *v.* stands for *vein.*)

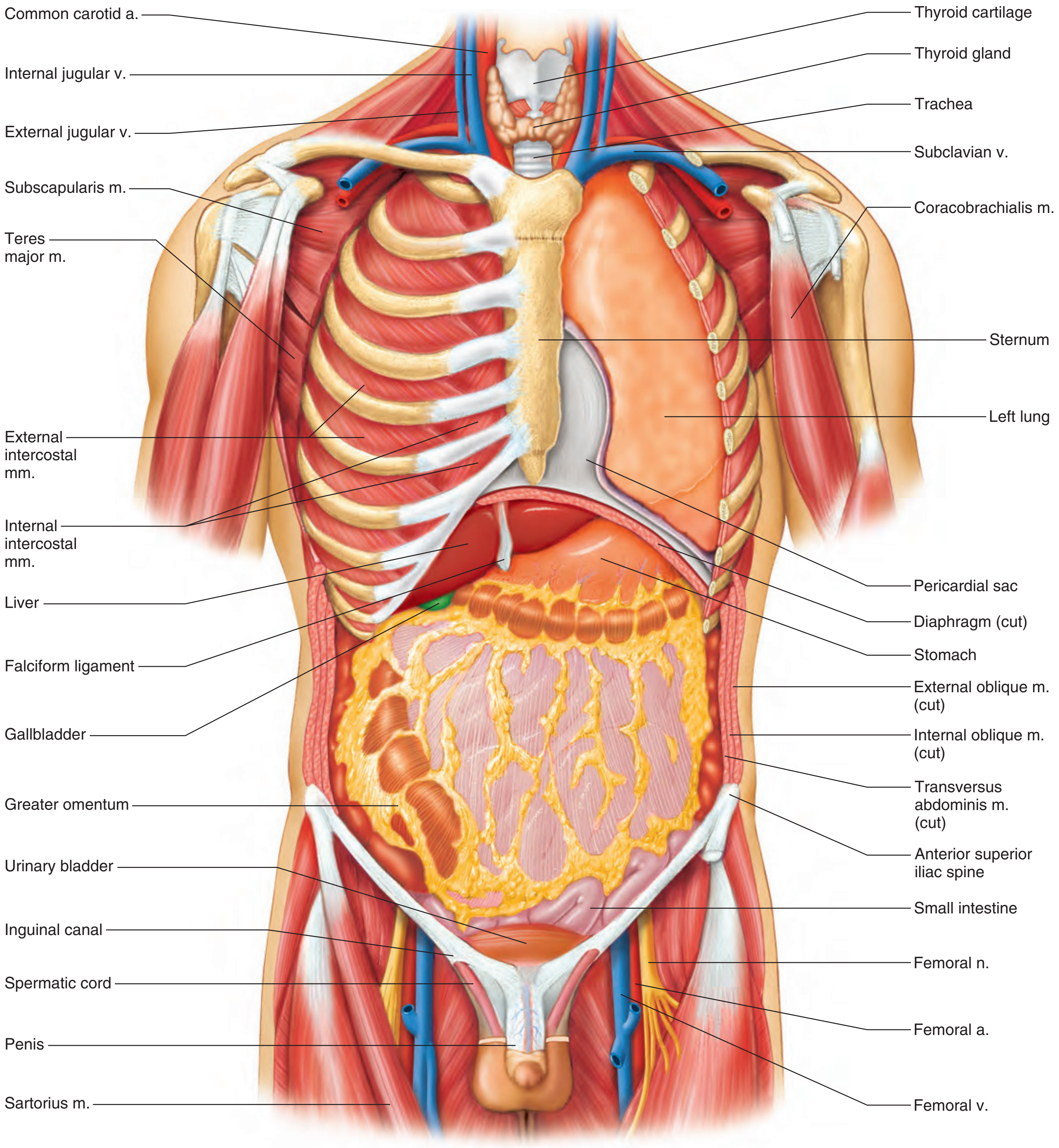

Common carotid a.
Internal jugular v.
External jugular v.
Subscapularis m.
Teres major m.
External intercostal mm.
Internal intercostal mm.
Liver
Falciform ligament
Gallbladder
Greater omentum
Urinary bladder
Inguinal canal
Spermatic cord
Penis
Sartorius m.
Thyroid cartilage
Thyroid gland
Trachea
Subclavian v.
Coracobrachialis m.
Sternum
Left lung
Pericardial sac
Diaphragm (cut)
Stomach
External oblique m. (cut)
Internal oblique m. (cut)
Transversus abdominis m. (cut)
Anterior superior iliac spine
Small intestine
Femoral n.
Femoral a.
Femoral v.

**PLATE THREE** Human male torso with the deep muscles removed and the abdominal viscera exposed. (*n.* stands for *nerve, a.* stands for *artery, m.* stands for *muscle, mm.* stands for muscles, and *v.* stands for *vein.*)

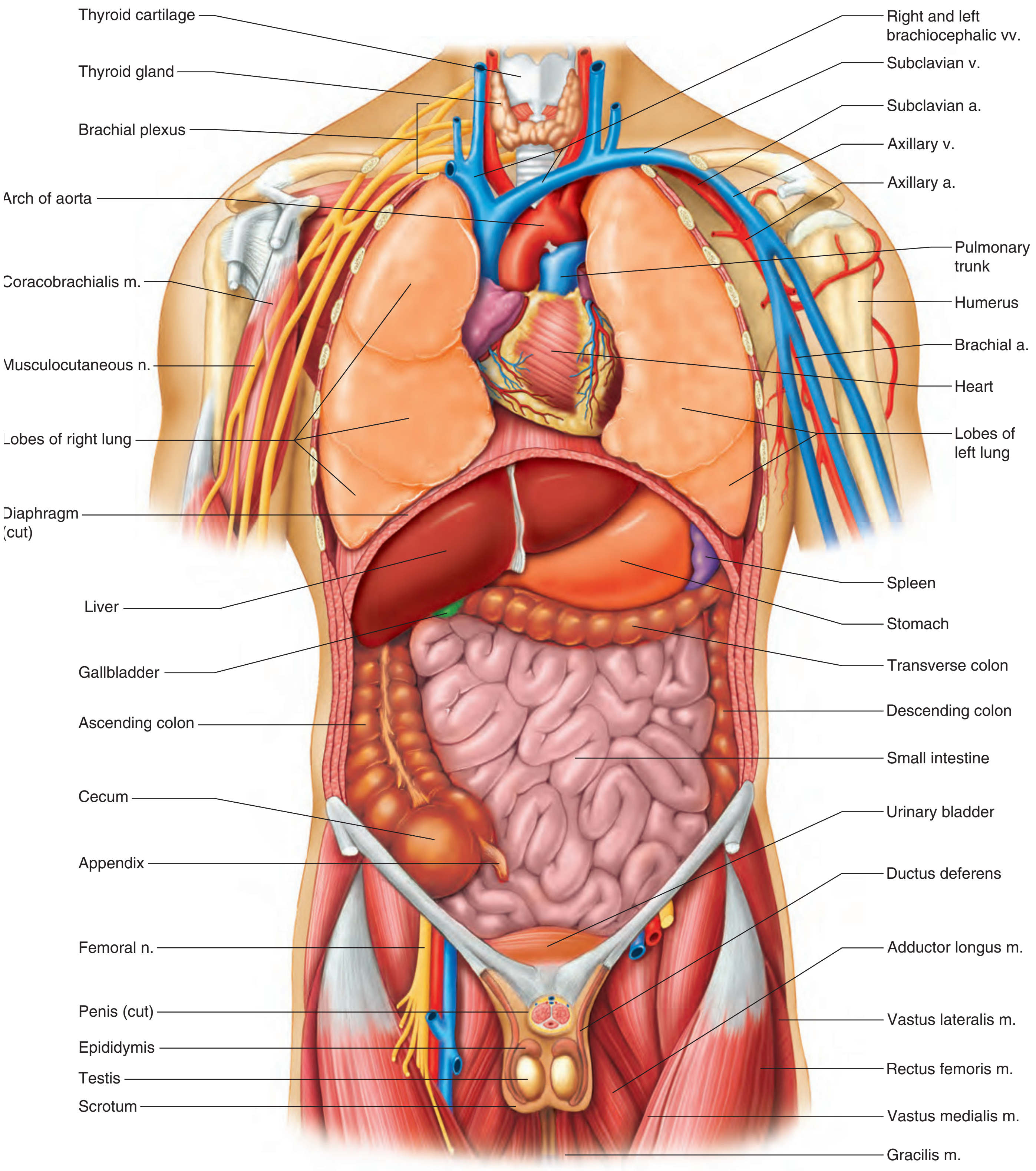

Thyroid cartilage
Thyroid gland
Brachial plexus
Arch of aorta
Coracobrachialis m.
Musculocutaneous n.
Lobes of right lung
Diaphragm (cut)
Liver
Gallbladder
Ascending colon
Cecum
Appendix
Femoral n.
Penis (cut)
Epididymis
Testis
Scrotum
Right and left brachiocephalic vv.
Subclavian v.
Subclavian a.
Axillary v.
Axillary a.
Pulmonary trunk
Humerus
Brachial a.
Heart
Lobes of left lung
Spleen
Stomach
Transverse colon
Descending colon
Small intestine
Urinary bladder
Ductus deferens
Adductor longus m.
Vastus lateralis m.
Rectus femoris m.
Vastus medialis m.
Gracilis m.

**PLATE FOUR** Human male torso with the thoracic and abdominal viscera exposed. (*n.* stands for *nerve, a.* stands for *artery, m.* stands for *muscle, v.* stands for *vein, and vv. stands for veins.*)

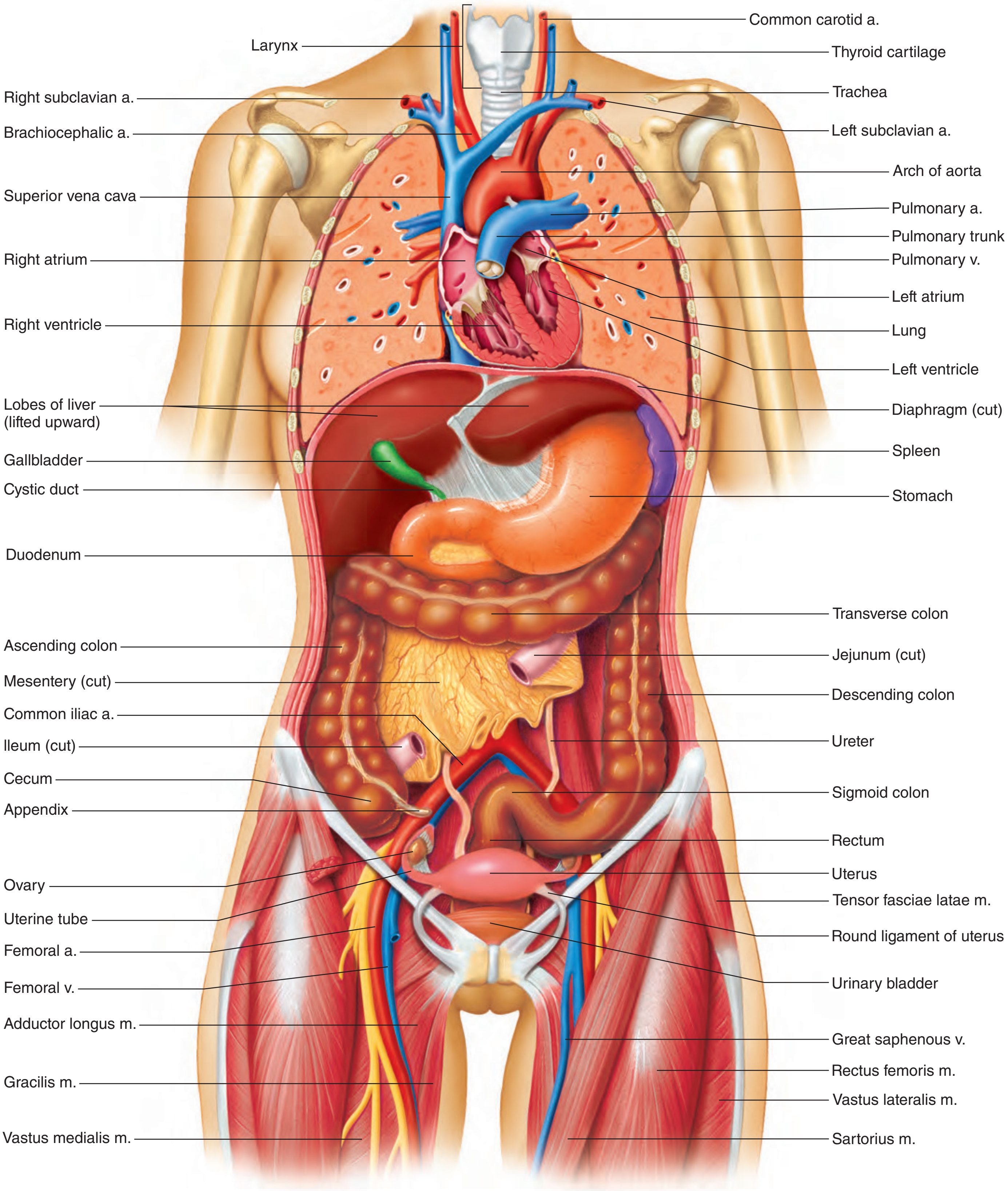

Common carotid a.
Larynx
Thyroid cartilage
Trachea
Right subclavian a.
Left subclavian a.
Brachiocephalic a.
Arch of aorta
Superior vena cava
Pulmonary a.
Pulmonary trunk
Right atrium
Pulmonary v.
Left atrium
Right ventricle
Lung
Left ventricle
Lobes of liver (lifted upward)
Diaphragm (cut)
Spleen
Gallbladder
Cystic duct
Stomach
Duodenum
Transverse colon
Ascending colon
Jejunum (cut)
Mesentery (cut)
Descending colon
Common iliac a.
Ureter
Ileum (cut)
Cecum
Sigmoid colon
Appendix
Rectum
Uterus
Ovary
Tensor fasciae latae m.
Uterine tube
Round ligament of uterus
Femoral a.
Urinary bladder
Femoral v.
Adductor longus m.
Great saphenous v.
Rectus femoris m.
Gracilis m.
Vastus lateralis m.
Vastus medialis m.
Sartorius m.

**PLATE FIVE** Human female torso with the lungs, heart, and small intestine sectioned and the liver reflected (lifted back). (*a.* stands for *artery, m.* stands for *muscle,* and *v.* stands for *vein.*)

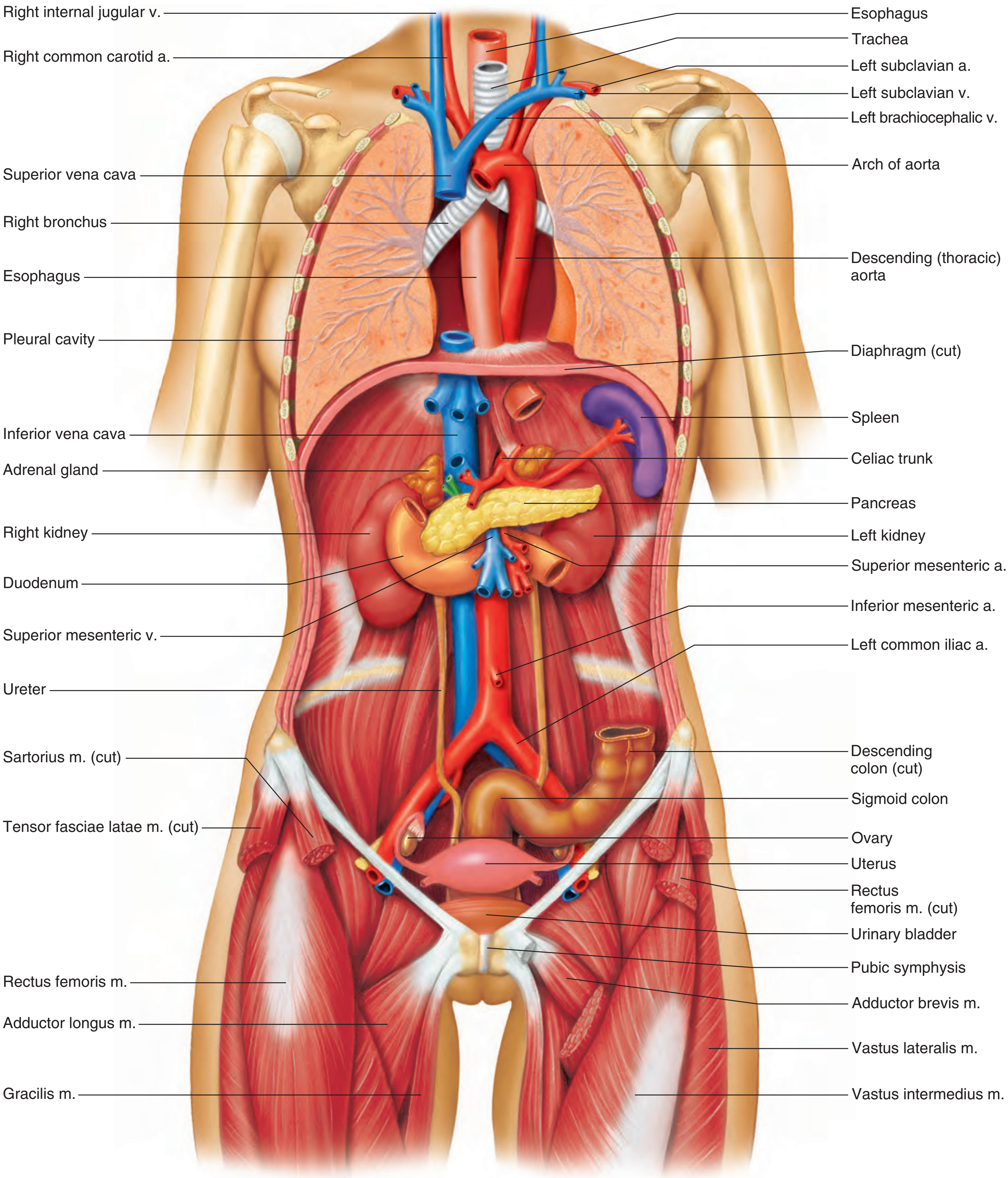

Right internal jugular v.
Right common carotid a.
Superior vena cava
Right bronchus
Esophagus
Pleural cavity
Inferior vena cava
Adrenal gland
Right kidney
Duodenum
Superior mesenteric v.
Ureter
Sartorius m. (cut)
Tensor fasciae latae m. (cut)
Rectus femoris m.
Adductor longus m.
Gracilis m.
Esophagus
Trachea
Left subclavian a.
Left subclavian v.
Left brachiocephalic v.
Arch of aorta
Descending (thoracic) aorta
Diaphragm (cut)
Spleen
Celiac trunk
Pancreas
Left kidney
Superior mesenteric a.
Inferior mesenteric a.
Left common iliac a.
Descending colon (cut)
Sigmoid colon
Ovary
Uterus
Rectus femoris m. (cut)
Urinary bladder
Pubic symphysis
Adductor brevis m.
Vastus lateralis m.
Vastus intermedius m.

**PLATE SIX** Human female torso with the heart, stomach, liver, and parts of the intestine and lungs removed. (*a.* stands for *artery, m.* stands for *muscle,* and *v.* stands for *vein.*)

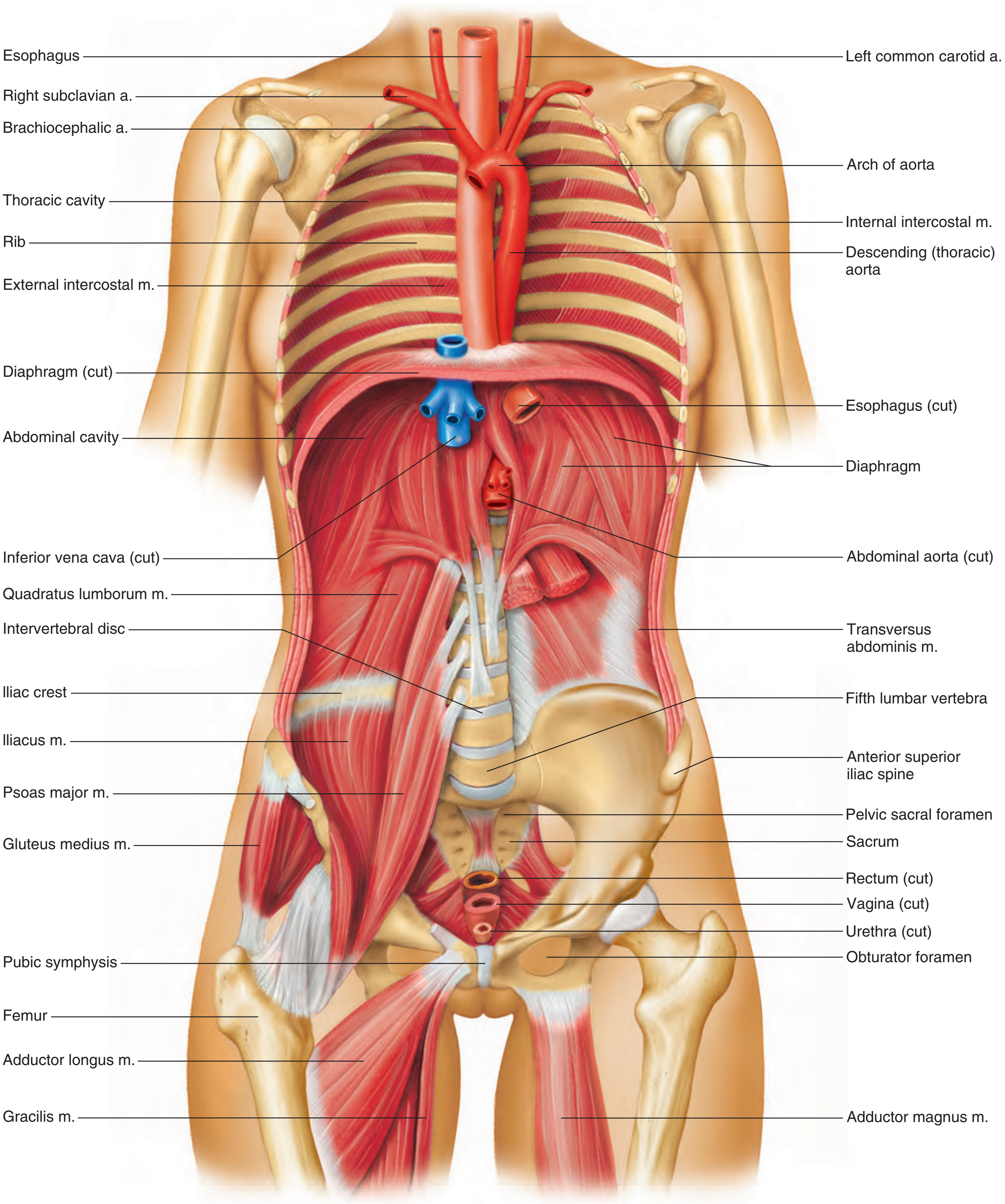
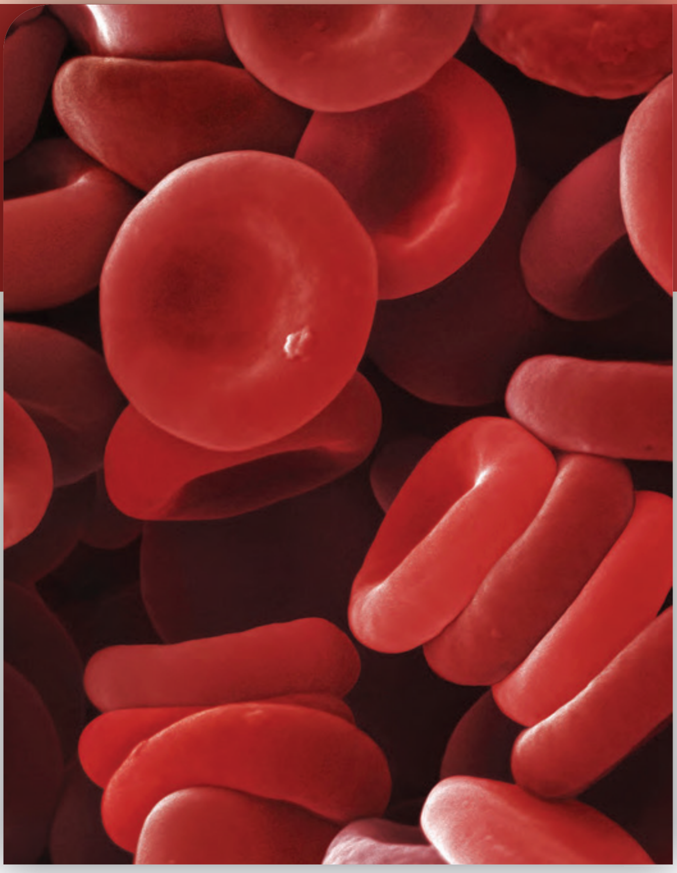

Esophagus
Right subclavian a.
Brachiocephalic a.
Thoracic cavity
Rib
External intercostal m.
Diaphragm (cut)
Abdominal cavity
Inferior vena cava (cut)
Quadratus lumborum m.
Intervertebral disc
Iliac crest
Iliacus m.
Psoas major m.
Gluteus medius m.
Pubic symphysis
Femur
Adductor longus m.
Gracilis m.
Left common carotid a.
Arch of aorta
Internal intercostal m.
Descending (thoracic) aorta
Esophagus (cut)
Diaphragm
Abdominal aorta (cut)
Transversus abdominis m.
Fifth lumbar vertebra
Anterior superior iliac spine
Pelvic sacral foramen
Sacrum
Rectum (cut)
Vagina (cut)
Urethra (cut)
Obturator foramen
Adductor magnus m.

**PLATE SEVEN** Human female torso with the thoracic, abdominal, and pelvic viscera removed. (*a.* stands for *artery,* and *m.* stands for *muscle.*)

# 2

# Chemical Basis of Life



*Much of the iron in the body is incorporated into hemoglobin in red blood cells.*

Iron overload. Too little or too much of just one type of body chemical can affect physiology and therefore health. This is the case for iron. The element iron is part of the protein hemoglobin, which carries oxygen to tissues, transported in red blood cells. Too little iron results in too few red blood cells and the great fatigue of anemia. Fatigue is also a consequence of the body having too much iron.

A complex set of signals oversees the fate of iron in the human body. Each day, cells lining the small intestine absorb 1 to 2 milligrams of iron from the diet into the bloodstream. Here, the iron circulates bound to a protein called transferrin and eventually becomes incorporated into hemoglobin in red blood cells. When old red blood cells break down, scavenger cells called macrophages capture the released iron, bind it to yet another protein, called ferritin, and then either store the iron or pass it to the liver for storage.

More than a dozen inherited "iron overload" diseases are known, each disrupting a different step in the body's handling of iron. Dietary absorption of iron may increase, for example, or more iron might be released into the circulation. If transferrin cannot accommodate a flood of iron, the element is deposited in certain cell types in the liver, heart, and pancreas. When this happens, there is a release of toxic forms of oxygen, called reactive oxygen species (ROS), which damage many of the types of molecules discussed in this chapter: lipids, proteins, and DNA. The extra iron and ROS overwhelm cells' antioxidant abilities, and irreversible damage results. In addition to chronic fatigue, the person may develop weak bones, joint pain, and diabetes. For some of the iron overload diseases, treatment is removing blood periodically and discarding it.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 2.1 Introduction

1. Give examples of how the study of living materials requires an understanding of chemistry. (p. 40)

### 2.2 Structure of Matter

2. Describe the relationships among matter, atoms, and molecules. (p. 40)
3. Describe how atomic structure determines how atoms interact. (p. 41)
4. Explain how molecular and structural formulas symbolize the composition of compounds. (p. 46)
5. Describe three types of chemical reactions. (p. 47)
6. Define acids, bases, and buffers. (p. 47)
7. Define pH and be able to use the pH scale. (p. 48)

### 2.3 Chemical Constituents of Cells

8. List the major inorganic chemicals in cells and identify the functions of each. (p. 49)
9. Describe the general functions of the four main groups of organic chemicals in cells. (p. 49)

**Module 2:**
Cells & Chemistry

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**di-** [two] *di*saccharide: Compound whose molecules are composed of two bonded sugar units.

**glyc-** [sweet] *glyc*ogen: Complex carbohydrate composed of many glucose molecules bonded in a particular way.

**lip-** [fat] *lip*ids: Group of organic compounds that includes fats.

**-lyt** [dissolvable] electro*lyt*e: Substance that releases ions in water.

**mono-** [one] *mono*saccharide: Compound whose molecule consists of a single sugar unit.

**poly-** [many] *poly*unsaturated: Molecule that has two or more double bonds between its carbon atoms.

**sacchar-** [sugar] mono*sacchar*ide: Molecule consisting of a single sugar unit.

**syn-** [together] *syn*thesis: Process by which substances join to form new types of substances.

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## 2.1 | Introduction

At the cellular level of organization, biology, in a sense, becomes chemistry. A cell's working parts—its organelles—are intricate assemblies of molecules. Because the molecules that build the cells that build tissues and organs are themselves composed of atoms, the study of anatomy and physiology begins with chemistry.

**Chemistry** is the branch of science that considers the composition of matter and how this composition changes. Understanding chemistry is essential for understanding anatomy and physiology because body structures and functions result from chemical changes within cells. Indeed, the human body is composed of chemicals, including salts, water, proteins, carbohydrates, lipids, and nucleic acids. All of the food that we eat, liquids that we drink, and medications that we may take when we are sick are chemicals.

## 2.2 | Structure of Matter

**Matter** is anything that has weight and takes up space. This includes all the solids, liquids, and gases in our surroundings, as well as inside our bodies. Matter consists of particles that are organized in specific ways.

Strictly speaking, matter has *mass* and takes up space. **Mass** refers to the amount of a substance, whereas **weight** refers to how heavy it is. If your weight on earth is 150 pounds, on the moon it would be only 25 pounds, but your mass would be the same in both places. That is, your composition is the same on the moon as it is on earth, but you weigh less on the moon, because the force of gravity is lower there. Because we are dealing with life on earth, and constant gravity, we can consider mass and weight as roughly equivalent. Many of our students find it easier to think in terms of weight rather than mass.

### Elements and Atoms

All matter is composed of fundamental substances called **elements** (el′ĕ-mentz). Examples include such common materials as iron, copper, silver, gold, aluminum, carbon, hydrogen, and oxygen. A few elements exist in a pure form, but most combine with other elements.

Living organisms require about twenty elements. Of these, oxygen, carbon, hydrogen, and nitrogen make up more than 95% (by weight) of the human body (table 2.1). As the table shows, a one- or two-letter symbol represents each element.

Elements are composed of particles called **atoms** (at′omz), which are the smallest complete units of ele-

**TABLE 2.1 Major Elements in the Body**

| Major Elements | Symbol | Approximate Percentage of the Human Body (by weight) |
|---|---|---|
| Oxygen | O | 65.0 |
| Carbon | C | 18.5 |
| Hydrogen | H | 9.5 |
| Nitrogen | N | 3.2 |
| Calcium | Ca | 1.5 |
| Phosphorus | P | 1.0 |
| Potassium | K | 0.4 |
| Sulfur | S | 0.3 |
| Chlorine | Cl | 0.2 |
| Sodium | Na | 0.2 |
| Magnesium | Mg | 0.1 |
| | | Total 99.9% |
| **Trace Elements** | | |
| Chromium | Cr | Together less than 0.1% |
| Cobalt | Co | |
| Copper | Cu | |
| Fluorine | F | |
| Iodine | I | |
| Iron | Fe | |
| Manganese | Mn | |
| Zinc | Zn | |

ments. Atoms of an element are similar to each other, but they differ from the atoms that make up other elements. Atoms of different elements vary in size, weight, and the ways they interact with atoms of other elements. Some atoms can combine with atoms like themselves or with other atoms by forming attractions called **chemical bonds,** whereas other atoms cannot form such bonds.

## Atomic Structure

An atom consists of a central portion, called the **nucleus,** and one or more **electrons** (e-lek′tronz) that constantly move around it. The nucleus contains one or more relatively large particles called **protons** (pro′tonz). The nucleus also usually contains one or more **neutrons** (nu′tronz), which are similar in size to protons.

Electrons, which are extremely small, each carry a single, negative electrical charge ($e^-$), whereas protons each carry a single, positive electrical charge ($p^+$). Neutrons are uncharged and thus are electrically neutral ($n^0$) (fig. 2.1).

Because the nucleus contains the protons, it is always positively charged. However, the number of electrons outside the nucleus equals the number of protons. Therefore, a complete atom is electrically uncharged, or neutral.

The atoms of different elements have different numbers of protons. The number of protons in the atoms of a particular element is called the element's **atomic number.** Hydrogen, for example, whose atoms each have one proton, has the atomic number 1; carbon, whose atoms each have six protons, has the atomic number 6.

The **atomic weight** of an atom of an element approximately equals the number of protons and neutrons in its nucleus (electrons have very little weight). Thus, the atomic weight of hydrogen, with one proton and no neutrons, is 1, whereas the atomic weight of carbon, with six protons and six neutrons, is 12 (table 2.2). In other words, an atom of carbon weighs twelve times more than an atom of hydrogen.

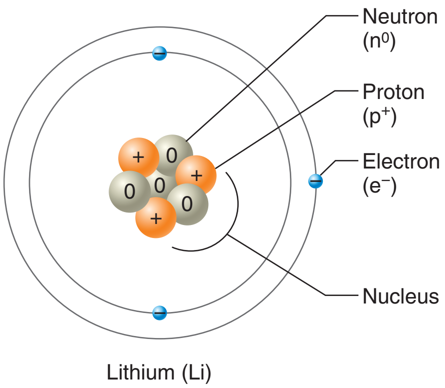


**FIGURE 2.1** AP|R An atom consists of subatomic particles. In an atom of the element lithium, three electrons move around a nucleus that consists of three protons and four neutrons.

All the atoms of a particular element have the same atomic number because they have the same number of protons and electrons. However, the atoms of an element vary in the number of neutrons in their nuclei; thus, they vary in atomic weight. For example, all oxygen atoms have eight protons in their nuclei, but these atoms may have eight, nine, or ten neutrons, corresponding to, respectively, atomic weights of 16, 17, and 18. Atoms of an element with different atomic weights are called **isotopes** (i′so-tōps) of that element. Because a sample of an element is likely to include more than one isotope, the atomic weight of the element is often considered to be the average weight of the isotopes present. (See Appendix D, Periodic Table of the Elements, p. 580.)

How atoms interact depends on their number of electrons. Because the number of electrons in an atom is equal to its number of protons, all the isotopes of a particular element have the same number of electrons and react chemically in the same manner. Therefore, any of the isotopes of oxygen can have the same function in an organism's metabolic reactions.

Isotopes may be stable, or they may have unstable atomic nuclei that decompose, releasing energy or pieces of themselves. Unstable isotopes are called *radioactive* because they emit energetic particles, and the energy or atomic fragments they give off are called *radiation.*

Three common forms of radiation are alpha ($\alpha$), beta ($\beta$), and gamma ($\gamma$). Alpha radiation consists of particles

### CAREER CORNER

### Pharmacy Technician

The flu season is in full force and the supermarket pharmacy line snakes all the way to the bakery. The pharmacy technician speedily yet carefully updates customers' records and processes insurance information, hands customers their prescriptions, and accepts payment. He or she can answer practical questions, such as when to take a medication, but asks the pharmacist to address health-related concerns.

In addition to these customer service skills, the pharmacy technician gathers information from health-care professionals or from patients about particular prescriptions, checks drug inventories, prepares ointments, counts pills, measures liquid medications, and packages and labels drug containers. The pharmacist verifies that the prescription has been prepared and labeled properly. The technician may also assist at special events, such as vaccination clinics and education sessions.

Pharmacy technicians work in stand-alone pharmacies, in supermarkets and big-box stores, in hospitals and skilled nursing facilities, and at mail-order dispensaries. A high school diploma and in some states a training program and certification are required to be a pharmacy technician. The job requires stamina, attention to detail to avoid errors, and a friendly approach to serving customers.

**TABLE 2.2** Atomic Structure of Elements 1 Through 12

| Element | Symbol | Atomic Number | Atomic Weight | Protons | Neutrons | Electrons in Shells | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | First | Second | Third |
| Hydrogen | H | 1 | 1 | 1 | 0 | 1 | | |
| Helium | He | 2 | 4 | 2 | 2 | 2 (inert) | | |
| Lithium | Li | 3 | 7 | 3 | 4 | 2 | 1 | |
| Beryllium | Be | 4 | 9 | 4 | 5 | 2 | 2 | |
| Boron | B | 5 | 11 | 5 | 6 | 2 | 3 | |
| Carbon | C | 6 | 12 | 6 | 6 | 2 | 4 | |
| Nitrogen | N | 7 | 14 | 7 | 7 | 2 | 5 | |
| Oxygen | O | 8 | 16 | 8 | 8 | 2 | 6 | |
| Fluorine | F | 9 | 19 | 9 | 10 | 2 | 7 | |
| Neon | Ne | 10 | 20 | 10 | 10 | 2 | 8 (inert) | |
| Sodium | Na | 11 | 23 | 11 | 12 | 2 | 8 | 1 |
| Magnesium | Mg | 12 | 24 | 12 | 12 | 2 | 8 | 2 |

from atomic nuclei, each of which includes two protons and two neutrons, that travel slowly and can weakly penetrate matter. Beta radiation consists of much smaller particles (electrons) that travel more rapidly and penetrate matter more deeply. Gamma radiation is similar to X-ray radiation and is the most penetrating of these forms.

Each kind of radioactive isotope produces one or more forms of radiation, and each becomes less radioactive at a particular rate. The time required for an isotope to lose one-half of its radioactivity is called its *half-life.* Thus, the isotope of iodine called iodine-131, which emits one-half of its radiation in 8.1 days, has a half-life of 8.1 days. Half-lives vary greatly. The half-life of phosphorus-32 is 14.3 days; that of cobalt-60 is 5.26 years; and that of radium-226 is 1,620 years. Clinical Application 2.1 discusses some practical applications of radioactive isotopes.

**PRACTICE**

1. What are elements?
2. Which elements are most common in the human body?
3. Where are electrons, protons, and neutrons located in an atom?
4. What is the difference between atomic number and atomic weight?

## Bonding of Atoms

Atoms can attach to other atoms by forming chemical bonds. The chemical behavior of atoms results from interactions among their electrons. When atoms form chemical bonds, they gain, lose, or share electrons. The electrons of an atom occupy one or more areas of space, called *shells,* around the nucleus (see table 2.2). For the elements up to atomic number 18, the maximum number of electrons that each of the first three inner shells can hold is as follows:

| | |
|---|---|
| First shell (closest to the nucleus) | 2 electrons |
| Second shell | 8 electrons |
| Third shell | 8 electrons |

More complex atoms may have as many as eighteen electrons in the third shell. Simplified diagrams, such as those in figure 2.2, depict electron locations within the shells of atoms.

The electrons in the outermost shell of an atom determine its chemical behavior. Atoms such as helium,

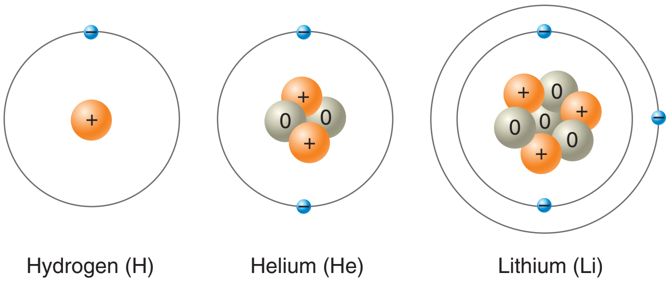


**FIGURE 2.2** Electrons orbit the atomic nucleus. The single electron of a hydrogen atom is located in its first shell. The two electrons of a helium atom fill its first shell. Two of the three electrons of a lithium atom are in the first shell, and one is in the second shell.

## CLINICAL APPLICATION 2.1

## Radioactive Isotopes: Helpful and Harmful

Radioactive chemicals are useful in studying life processes and in diagnosing and treating some diseases. Atomic radiation is detected with special equipment, such as a scintillation counter (fig. 2A). A radioactive isotope can be introduced into an organism and then traced as it enters into metabolic activities. For example, the human thyroid gland is unique in using the element iodine in its metabolism. Therefore, radioactive iodine-131 is used to study thyroid functions and to evaluate thyroid disease (fig. 2B). Doctors use thallium-201, which has a half-life of 73.5 hours, to assess heart conditions, and gallium-67, with a half-life of 78 hours, to detect and monitor the progress of certain cancers and inflammatory diseases.

Atomic radiation also can change chemical structures and in this way alter vital cellular processes. For this reason, doctors sometimes use radioactive isotopes, such as cobalt-60, to treat cancers. The radiation from the cobalt preferentially kills the rapidly dividing cancer cells.

Exposure to radiation can cause disease, such as certain cancers. The transfer of energy as radiation is emitted damages DNA in ways that kill cells or make them cancerous. Exposure to ultraviolet radiation in sunlight, for example, causes skin cancer, and excess medical X rays or gamma rays increase the risk of developing cancer in certain body parts.

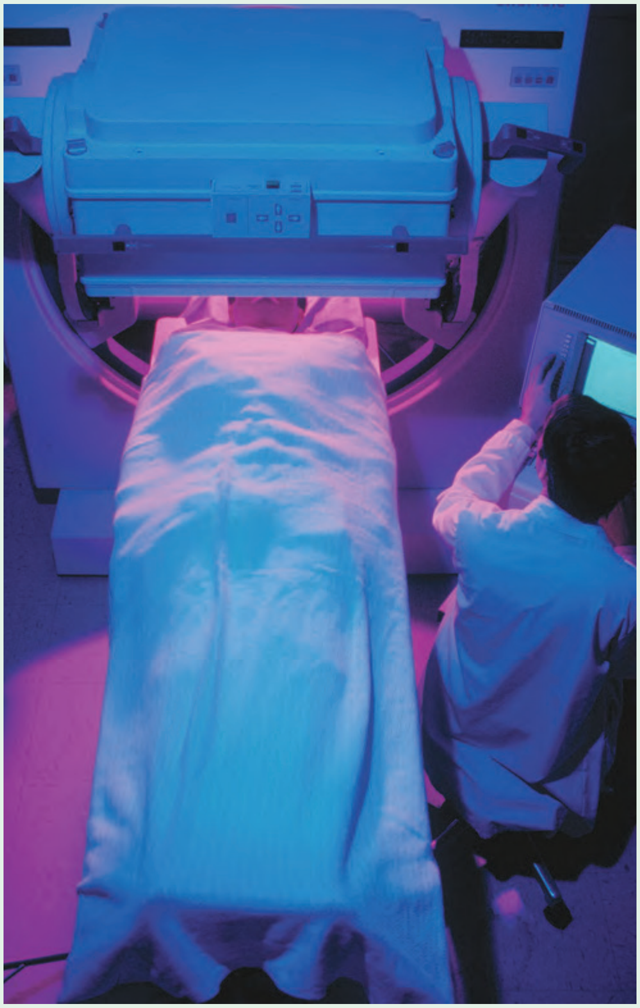


**FIGURE 2A** Scintillation counters detect radioactive isotopes.

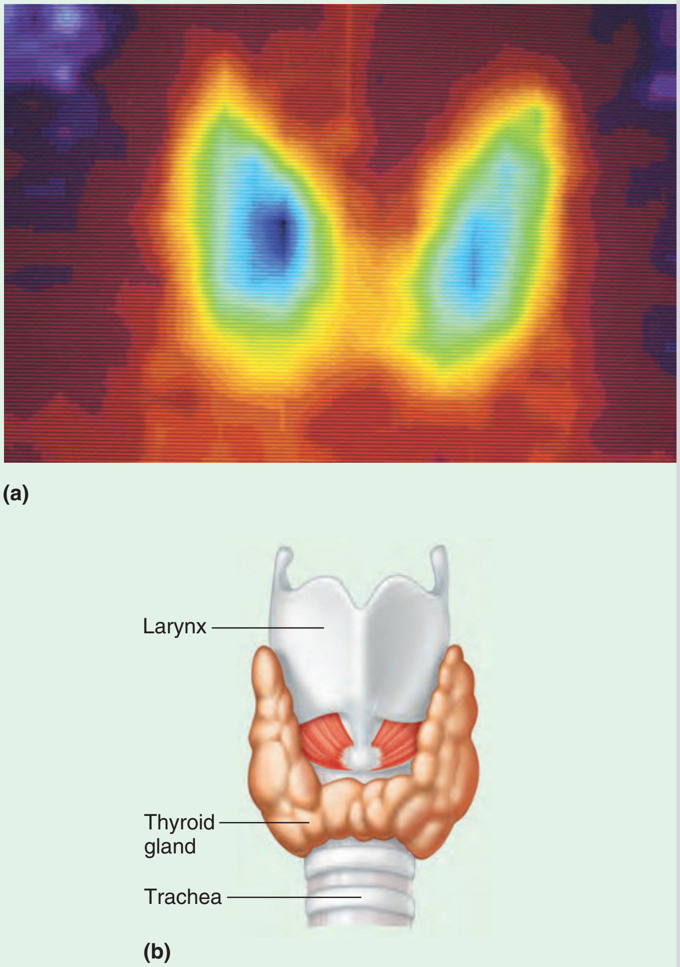


**FIGURE 2B** **(a)** Scan of the thyroid gland 24 hours after the patient received radioactive iodine. Note how closely the scan in **(a)** resembles the shape of the thyroid gland, shown in **(b)**.

whose outermost electron shells are filled, have stable structures and are chemically inactive, or **inert** (see table 2.2). Atoms such as hydrogen or lithium, whose outermost electron shells are incompletely filled, tend to gain, lose, or share electrons in ways that empty or fill their outer shells. This enables them to achieve stable structures.

Atoms that gain or lose electrons become electrically charged and are called **ions** (i′onz). An atom of sodium, for example, has eleven electrons: two in the first shell, eight in the second shell, and one in the third shell (fig. 2.3). This atom tends to lose the electron from its outer shell, which leaves the second (now the outermost) shell filled and the new form stable (fig. 2.4*a*). In the process, sodium is left with eleven protons ($11^+$) in its nucleus and only ten electrons ($10^-$). As a result, the atom develops a net electrical charge of +1 and is called a sodium ion, symbolized $Na^+$.

A chlorine atom has seventeen electrons, with two in the first shell, eight in the second shell, and seven in the third shell. An atom of this type tends to accept a single electron, filling its outer shell and achieving stability (fig. 2.4*a*). In the process, the chlorine atom is left with seventeen protons ($17^+$) in its nucleus and eighteen electrons ($18^-$). The atom develops a net electrical charge of –1 and is called a chloride ion, symbolized $Cl^-$.

Because oppositely charged ions attract, sodium and chloride ions react to form a type of chemical bond called an **ionic bond** (electrovalent bond). Sodium ions ($Na^+$) and chloride ions ($Cl^-$) unite in this manner to form sodium chloride (NaCl), or table salt (fig. 2.4*b*). Some ions have an electrical charge greater than 1—for example, $Ca^{+2}$ (or $Ca^{++}$).

Ionically bound substances do not form discrete molecules—instead, they form arrays, such as crystals of sodium chloride (fig. 2.4*c*). Atoms may also bond by sharing electrons rather than by exchanging them. A hydrogen atom, for example, has one electron in its first shell but requires two electrons to achieve a stable structure (fig. 2.5). It may fill this shell by combining with another hydrogen atom in such a way that the two atoms share a pair of electrons. The two electrons then encircle the nuclei of both atoms, and each atom achieves a stable form. The chemical bond

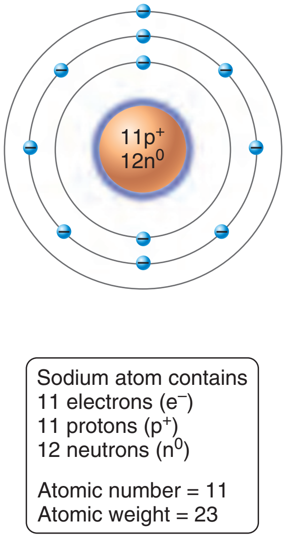
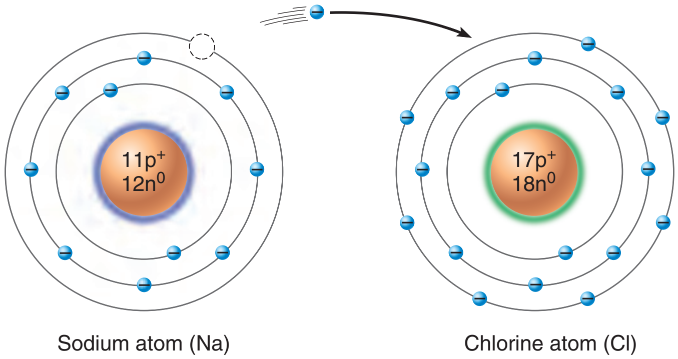
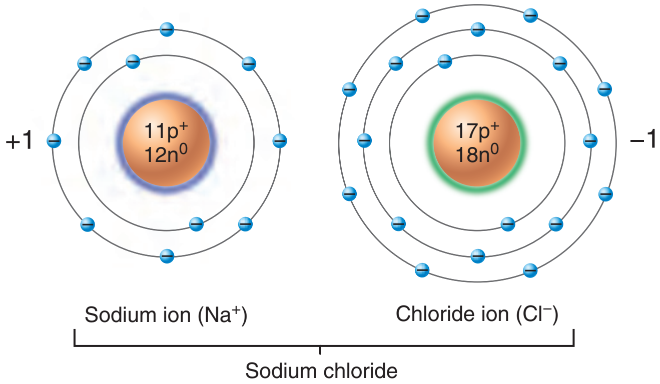


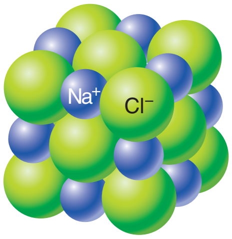
**FIGURE 2.3** A sodium atom.



**(a)** Separate atoms
If a sodium atom loses an electron to a chlorine atom, the sodium atom becomes a sodium ion ($Na^+$), and the chlorine atom becomes a chloride ion ($Cl^-$).



**(b)** Bonded ions
These oppositely charged particles attract electrically and join by an ionic bond.



**(c)** Salt crystal
Ionically bonded substances form arrays such as a crystal of NaCl.

**FIGURE 2.4** An ionic bond forms when one atom gains and another atom loses electrons **(a)** and then oppositely charged ions attract **(b)**. Ionically bonded substances may form crystals **(c)**.

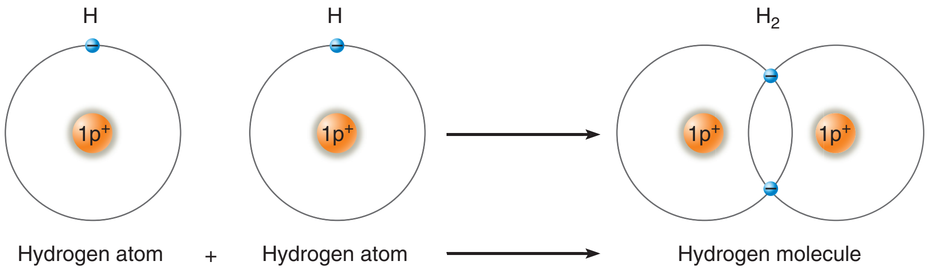


**FIGURE 2.5** A hydrogen molecule forms when two hydrogen atoms share a pair of electrons. A covalent bond forms between the atoms.

between the atoms that share electrons is called a **covalent bond.**

Carbon atoms, which have two electrons in their first shells and four electrons in their second shells, can form covalent bonds with each other and with other atoms. In fact, carbon atoms (and certain other atoms) may bond in such a way that two atoms share one or more pairs of electrons. If one pair of electrons is shared, the resulting bond is called a *single covalent bond;* if two pairs of electrons are shared, the bond is called a *double covalent bond. Triple covalent bonds* are also possible between some atoms.

In ionic bonds, one or more electrons of one atom are pulled entirely toward another. In covalent bonds, atoms share electrons equally. In between these two extremes lies the covalent bond in which electrons are shared, but are not shared equally, such that the shared electrons move more toward one of the bonded atoms. This results in a molecule with an uneven distribution of charges. Such a molecule is called **polar.** Unlike an ion, a polar molecule has an equal number of protons and electrons, but more of the electrons are at one end of the molecule, making that end slightly negative, while the other end of the molecule is slightly positive. Typically, polar covalent bonds form where hydrogen atoms bond to oxygen or nitrogen atoms. Water is an important polar molecule (fig. 2.6*a*).

The attraction of the positive hydrogen end of a polar molecule to the negative nitrogen or oxygen end of another polar molecule is called a **hydrogen bond.** Hydrogen bonds are relatively weak. For example, below 0°C the hydrogen bonds between the water molecules shown in figure 2.6*b* are strong enough to form ice. Above 0°C, however, increased molecular movement breaks the hydrogen bonds, and water becomes a liquid. At body temperature (37°C), hydrogen bonds are important in protein and nucleic acid structure. In these cases, many hydrogen bonds form between polar regions of different parts of a single, very large molecule (see figs. 2.18 and 2.21*b*). Together, these individually weak bonds provide strength. The contribution of hydrogen bonds to protein and nucleic acid structure is described in section 2.3, pages 53 and 55.

## Molecules and Compounds

When two or more atoms bond, they form a new kind of particle called a **molecule** (mol′ĕ-kūl). If atoms of the same element bond, they produce molecules of that element. Gases of hydrogen, oxygen, and nitrogen consist of such molecules (see fig. 2.5).

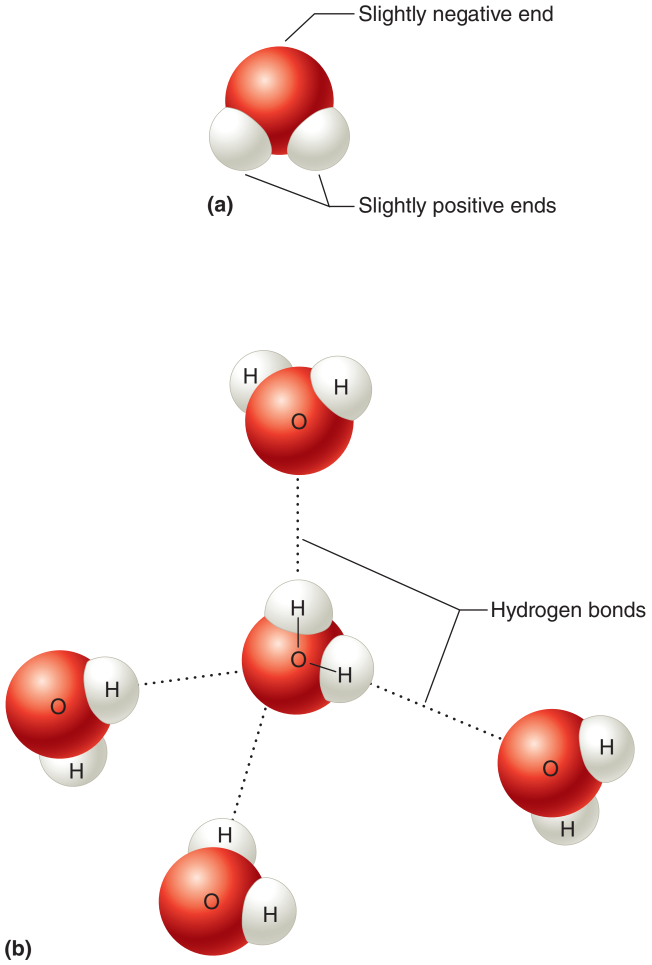


**FIGURE 2.6** APR Water is a polar molecule. **(a)** Water molecules have equal numbers of electrons and protons but are polar because the electrons are shared unequally, creating slightly negative ends and slightly positive ends. **(b)** Hydrogen bonding connects water molecules.

When atoms of different elements bond, they form molecules called **compounds.** Two atoms of hydrogen, for example, can bond with one atom of oxygen to produce a molecule of the compound water ($H_2O$) (fig. 2.7). Table sugar (*sucrose*), baking soda, natural gas, beverage alcohol, and most drugs are compounds.

A molecule of a compound always consists of definite kinds and numbers of atoms. A molecule of water, for instance, always has two hydrogen atoms and one oxygen atom. If two hydrogen atoms bond with two oxygen atoms, the compound formed is not water, but hydrogen peroxide ($H_2O_2$). Table 2.3 summarizes the characteristics of the particles of matter discussed so far.

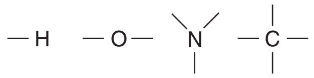
## PRACTICE

5. What is an ion?
6. Describe two ways that atoms bond with other atoms.
7. Distinguish between an ion and a polar molecule.
8. Distinguish between a molecule and a compound.

## Formulas

A **molecular formula** (mo-lek′u-lar for′mu-lah) represents the numbers and types of atoms in a molecule. Such a formula displays the symbols for the elements in the molecule and the number of atoms of each element. For example, the molecular formula for water is $H_2O$, which means that each water molecule consists of two atoms of hydrogen and one atom of oxygen (fig. 2.8). The molecular formula for the sugar *glucose* is $C_6H_{12}O_6$, indicating that each glucose molecule consists of six atoms of carbon, twelve atoms of hydrogen, and six atoms of oxygen.

Usually, the atoms of each element form a specific number of covalent bonds. Hydrogen atoms form single bonds, oxygen atoms form two bonds, nitrogen atoms form three bonds, and carbon atoms form four bonds. Symbols and lines depict bonds as follows:



These representations show how atoms are joined and arranged in molecules. Single lines represent single bonds, and double lines represent double bonds. Illustrations of this type are called **structural formulas** (struk′cher-al for′mu-lahz) (fig. 2.8). Three-dimensional models of structural formulas use different colors for the different kinds of atoms (fig. 2.9).

**TABLE 2.3 Some Particles of Matter**

| Particle | Characteristics |
|---|---|
| Atom | Smallest particle of an element that has the properties of that element |
| Electron ($e^-$) | Extremely small particle; carries a negative electrical charge and is in constant motion around the nucleus of an atom |
| Proton ($p^+$) | Relatively large particle; carries a positive electrical charge and is found within the nucleus of an atom |
| Neutron ($n^0$) | Relatively large particle; uncharged and thus electrically neutral; found within the nucleus of an atom |
| Molecule | Particle formed by the chemical union of two or more atoms |
| Ion | Atom or molecule that is electrically charged because it has gained or lost one or more electrons |

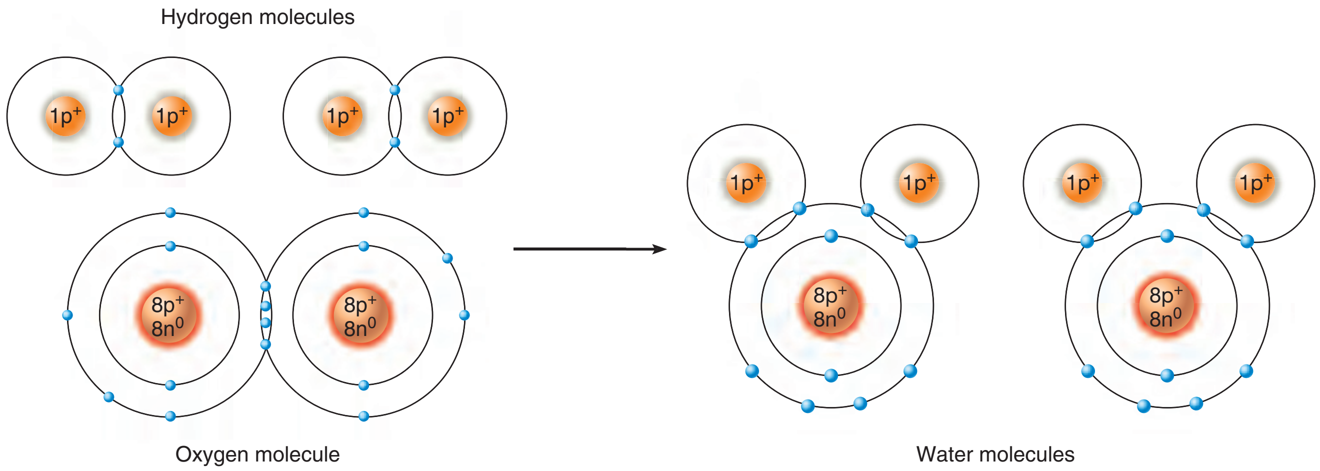


**FIGURE 2.7** Hydrogen molecules can combine with oxygen molecules, forming water molecules. The shared electrons represent covalent bonds.

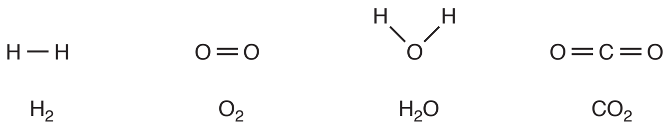


**FIGURE 2.8** Structural and molecular formulas for molecules of hydrogen, oxygen, water, and carbon dioxide. Note the double covalent bonds. (Triple covalent bonds are also possible between some atoms.)

## Chemical Reactions

Chemical reactions form or break bonds between atoms, ions, or molecules, generating new chemical combinations. For example, when two or more atoms (reactants) bond to form a more complex structure (product), the reaction is called **synthesis** (sin′thĕ-sis). Such a reaction is symbolized in this way:

$$A + B \longrightarrow AB$$

If the bonds within a reactant molecule break so that simpler molecules, atoms, or ions form, the reaction is called **decomposition** (de″kom-po-zish′un). Decomposition is symbolized as follows:

$$AB \longrightarrow A + B$$

Synthesis, which requires energy, is particularly important in the growth of body parts and the repair of worn or damaged tissues, which require buildup of larger molecules from smaller ones. In contrast, decomposition occurs when food molecules are digested into smaller ones that can be absorbed.

A third type of chemical reaction is an **exchange reaction.** In this reaction, parts of two different types of molecules trade positions as bonds are broken and new bonds are formed. The reaction is symbolized as follows:

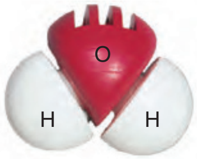
$$AB + CD \longrightarrow AD + CB$$

An example of an exchange reaction is when an acid reacts with a base, producing water and a salt. Acids and bases are described in the next section.

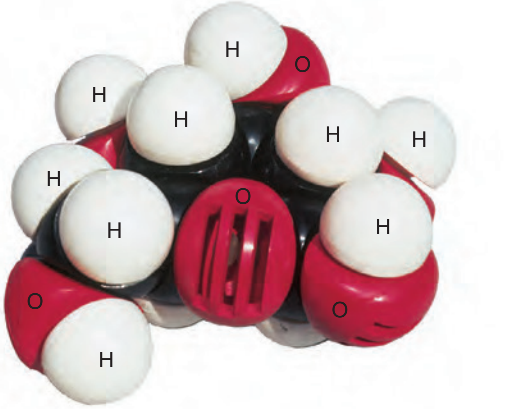
Many chemical reactions are reversible. This means that the product (or products) of the reaction can change back to the reactant (or reactants) that originally underwent the reaction. A **reversible reaction** is symbolized with a double arrow:

$$A + B \rightleftharpoons AB$$

Whether a reversible reaction proceeds in one direction or the other depends on such factors as the relative proportions of the reactant (or reactants) and product (or products), as well as the amount of available energy. Particular atoms or molecules that can change the rate (not the direction) of a reaction without being consumed in the process, called **catalysts,** speed many chemical reactions in the body so that they proceed fast enough to sustain the activities of life.



**(a)** A water molecule ($H_2O$), with the white parts depicting hydrogen atoms and the red part representing oxygen.



**(b)** A glucose molecule ($C_6H_{12}O_6$), in which the black parts represent carbon atoms.

**FIGURE 2.9** Three-dimensional molecular models depict spatial relationships of the constituent atoms.

## Acids and Bases

When ionically bound substances are placed in water, the slightly negative and positive ends of the water molecules cause the ions to leave each other and interact with the water molecules instead. For example, the salt sodium chloride (NaCl) releases sodium ions ($Na^+$) and chloride ions ($Cl^-$) when it is placed in water:

$$NaCl \longrightarrow Na^+ + Cl^-$$

In this way, the polarity of water dissociates salts in the internal environment (fig. 2.10). Because the resulting solution contains electrically charged particles (ions), it will conduct an electric current. Substances that release ions in water are, therefore, called **electrolytes** (e-lek′tro-lītz).

**Acids** are electrolytes that release hydrogen ions ($H^+$) in water. For example, in water, the compound hydrochloric acid (HCl) releases hydrogen ions ($H^+$) and chloride ions ($Cl^-$):

$$HCl \longrightarrow H^+ + Cl^-$$

Electrolytes that release ions that bond with hydrogen ions are called **bases.** For example, the compound sodium hydroxide (NaOH) releases hydroxide ions ($OH^-$) when placed in water (Note: Some ions, such as $OH^-$, consist of two or more atoms.):

$$NaOH \longrightarrow Na^+ + OH^-$$

The hydroxide ions, in turn, can bond with hydrogen ions to form water; thus, sodium hydroxide is a base. Many

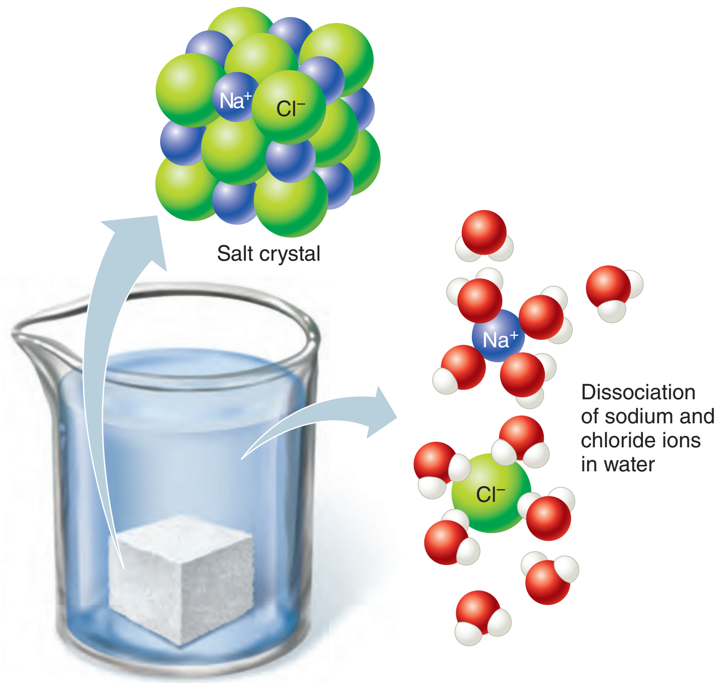

Na+
Cl−
Salt crystal
Na+
Cl−
Dissociation of sodium and chloride ions in water

**FIGURE 2.10** APR The polar nature of water molecules dissociates sodium chloride (NaCl) in water, releasing sodium ions ($Na^+$) and chloride ions ($Cl^-$).

bases are present in the body fluids, but because of the way they react in water, the concentration of hydroxide ions is a good estimate of the total base concentration.

The concentrations of hydrogen ions ($H^+$) and hydroxide ions ($OH^-$) in body fluids greatly affect the chemical reactions that control certain physiological functions, such as blood pressure and breathing rate. Because their concentrations are inversely related (if one goes up, the other goes down), keeping track of one of them provides information on the other as well. A value called **pH** measures hydrogen ion concentration.

The pH scale ranges from 0 to 14. A solution with a pH of 7.0, the midpoint of the scale, contains equal numbers of hydrogen and hydroxide ions and is said to be *neutral.* A solution that contains more hydrogen ions than hydroxide ions has a pH less than 7.0 and is *acidic.* A solution with fewer hydrogen ions than hydroxide ions has a pH greater than 7.0 and is *basic* (alkaline).

Figure 2.11 indicates the pH values of some common substances. Each whole number on the pH scale represents a tenfold difference in hydrogen ion concentration, and as the hydrogen ion concentration increases, the pH number gets smaller. Thus, a solution with a pH of 6 has ten times the hydrogen ion concentration of a solution with a pH of 7. This means that relatively small changes in pH can reflect large changes in hydrogen ion concentration.

**Buffers** are chemicals that resist pH change. They combine with hydrogen ions when these ions are in excess, or they donate hydrogen ions when these ions are depleted. Buffers and the regulation of the hydrogen ion concentration in body fluids are discussed further in chapter 18 (pp. 510–511).

The pH of human blood is about 7.4, and ranges from 7.35 to 7.45 (see fig. 2.11). If the pH drops below 7.35, the person has *acidosis;* if it rises above 7.45, the condition is *alkalosis*. Without medical intervention, a person usually cannot survive if blood pH drops to 6.9 or rises to 7.8 for more than a few hours. Homeostatic mechanisms such as those described in chapter 1 (p. 14) regulate pH of the internal environment.

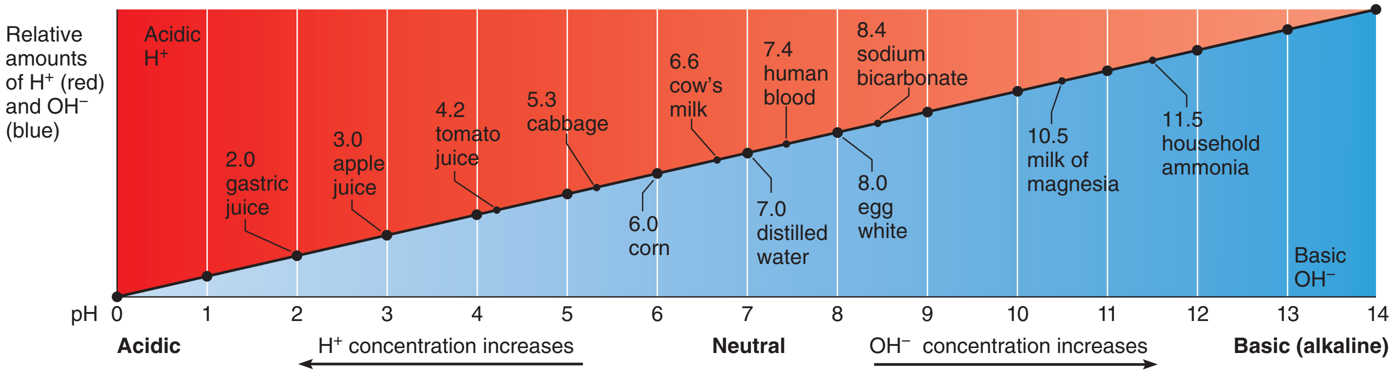


**FIGURE 2.11** The pH scale measures hydrogen ion ($H^+$) concentration. As the concentration of $H^+$ increases, a solution becomes more acidic, and the pH value decreases. As the concentration of ions that bond with $H^+$ (such as hydroxide ions) increases, a solution becomes more basic (alkaline), and the pH value increases. The pH values of some common substances are shown.

Q *What is the pH of the internal environment?*

**Answer can be found in Appendix F on page 582.**

## PRACTICE

9. What is a molecular formula? A structural formula?
10. Describe three kinds of chemical reactions.
11. Compare the characteristics of an acid with those of a base.
12. What does pH measure?
13. What is a buffer?

---

## 2.3 | Chemical Constituents of Cells

Chemicals, including those that enter into metabolic reactions or are produced by them, can be divided into two large groups. Chemicals that include both carbon and hydrogen atoms are called **organic** (or-gan′ik). The rest are **inorganic** (in″or-gan′ik).

Inorganic substances usually dissolve in water and dissociate to release ions; therefore, they are *electrolytes.* Many organic compounds also dissolve in water, but they are more likely to dissolve in organic liquids, such as ether or alcohol. Organic substances that dissolve in water usually do not release ions and are therefore called *nonelectrolytes.*

### Inorganic Substances

Among the inorganic substances common in cells are water, oxygen, carbon dioxide, and a group of compounds called salts.

#### *Water*

Water is the most abundant compound in living material and accounts for about two-thirds of the weight of an adult human. It is the major component of blood and other body fluids, including those in cells.

Water is an important *solvent* because many substances readily dissolve in it. A substance dissolved in a liquid, such as water, is called a *solute.* When it dissolves it is broken down into smaller and smaller pieces, eventually to molecular-sized particles, which may be ions. If two or more types of solutes are dissolved, they are much more likely to react with one another than were the original large pieces. Consequently, most metabolic reactions occur in water.

Water also plays an important role in moving chemicals in the body. For example, blood, which is mostly water, carries many vital substances, such as oxygen, sugars, salts, and vitamins, from the organs of digestion and respiration to the body cells.

Water can absorb and transport heat. Blood carries heat released from muscle cells during exercise from deeper parts of the body to the surface, where it may be lost to the outside.

#### *Oxygen*

Molecules of oxygen ($O_2$) enter the body through the respiratory organs and are transported throughout the body by the blood. The red blood cells bind and carry most of the oxygen. Cellular organelles use oxygen to release energy from the sugar glucose and other nutrients. The released energy drives the cell's metabolic activities.

#### *Carbon Dioxide*

Carbon dioxide ($CO_2$) is a simple, carbon-containing compound of the inorganic group. It is produced as a waste product when certain metabolic processes release energy, and it is then exhaled from the lungs.

#### *Salts*

A salt is a compound composed of oppositely charged ions, such as sodium ($Na^+$) and chloride ($Cl^-$), which is the familiar table salt NaCl. Salts are abundant in tissues and fluids. They provide many necessary ions, including sodium ($Na^+$), chloride ($Cl^-$), potassium ($K^+$), calcium ($Ca^{+2}$), magnesium ($Mg^{+2}$), phosphate ($PO_4^{-3}$), carbonate ($CO_3^{-2}$), bicarbonate ($HCO_3^-$), and sulfate ($SO_4^{-2}$). These ions are important in metabolic processes, including transport of substances into and out of cells, muscle contraction, and impulse conduction in nerve cells. Table 2.4 summarizes the functions of some of the inorganic substances in the body.

## PRACTICE

14. How do inorganic and organic molecules differ?
15. How do electrolytes and nonelectrolytes differ?
16. Name the inorganic substances common in body fluids.

---

### Organic Substances

Important groups of organic chemicals in cells include carbohydrates, lipids, proteins, and nucleic acids.

#### *Carbohydrates*

**Carbohydrates** (kar″bo-hi′drātz) provide much of the energy that cells require. They supply materials to build certain cell structures and often are stored as reserve energy supplies.

Carbohydrate molecules consist of atoms of carbon, hydrogen, and oxygen. These molecules usually have twice as many hydrogen as oxygen atoms—the same ratio of hydrogen to oxygen as in water molecules ($H_2O$). This ratio is easy to see in the molecular formula of the carbohydrate glucose ($C_6H_{12}O_6$).

The number of carbon atoms in a carbohydrate molecule varies with the type of carbohydrate. Among the smallest carbohydrates are **sugars.**

Sugars with 6 carbon atoms (hexoses) are examples of *simple sugars,* or **monosaccharides** (mon″o-sak′ah-rīdz). The simple sugars include glucose, fructose, and

**TABLE 2.4** Inorganic Substances Common in the Body

| Substance | Symbol or Formula | Functions |
|---|---|---|
| I. Inorganic molecules | | |
| Water | $H_2O$ | Major component of body fluids (chapter 1, p. 13); medium in which most biochemical reactions occur (chapter 2, p. 47); transports chemicals (chapter 12, p. 328); helps regulate body temperature (chapter 6, p. 136) |
| Oxygen | $O_2$ | Used in energy release from glucose molecules (chapter 4, p. 91) |
| Carbon dioxide | $CO_2$ | Waste product that results from metabolism (chapter 4, p. 91); reacts with water to form carbonic acid (chapter 16, p. 472) |
| II. Inorganic ions | | |
| Bicarbonate ions | $HCO_3^-$ | Helps maintain acid-base balance (chapter 18, p. 511) |
| Calcium ions | $Ca^{+2}$ | Necessary for bone development (chapter 7, p. 148), muscle contraction (chapter 8, p. 195), and blood clotting (chapter 12, p. 340) |
| Carbonate ions | $CO_3^{-2}$ | Component of bone tissue (chapter 7, p. 152) |
| Chloride ions | $Cl^-$ | Helps maintain water balance (chapter 18, p. 509) |
| Magnesium ions | $Mg^{+2}$ | Component of bone tissue (chapter 7, p. 152); required for certain metabolic processes (chapter 15, p. 444) |
| Phosphate ions | $PO_4^{-3}$ | Required for synthesis of ATP, nucleic acids, and other vital substances (chapter 4, pp. 91–94); component of bone tissue (chapter 7, p. 152); helps maintain polarization of cell membranes (chapter 9, p. 233) |
| Potassium ions | $K^+$ | Required for polarization of cell membranes (chapter 9, p. 233) |
| Sodium ions | $Na^+$ | Required for polarization of cell membranes (chapter 9, p. 233); helps maintain water balance (chapter 11, p. 315) |
| Sulfate ions | $SO_4^{-2}$ | Helps maintain polarization of cell membranes (chapter 9, p. 233) |

galactose, as well as the 5-carbon sugars ribose and deoxyribose. Figure 2.12 illustrates the structural formulas of glucose.

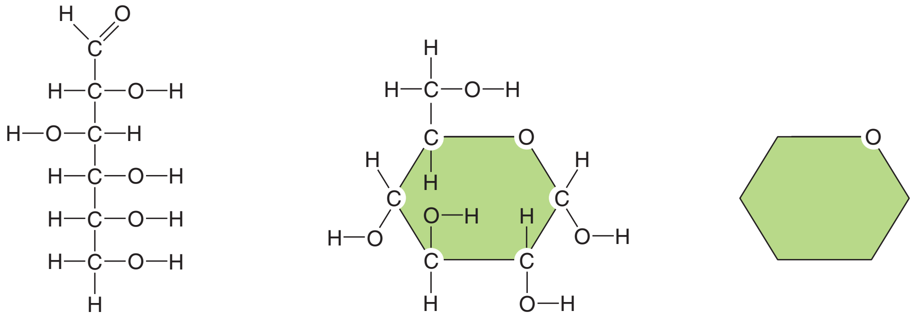
In *complex carbohydrates,* a number of simple sugar molecules link to form molecules of different sizes (fig. 2.13). Some complex carbohydrates, such as sucrose (table sugar) and lactose (milk sugar), are *double sugars,* or **disaccharides** (di-sak′ah-rīdz), whose molecules each consist of two simple sugar building blocks. Other complex carbohydrates are made up of many simple sugar units joined to form **polysaccharides** (pol″e-sak′ah-rīdz), such as plant starch. Animals, including humans, synthesize a polysaccharide similar to starch called *glycogen.*

### *Lipids*

**Lipids** (lip′idz) are organic substances that are insoluble in water but soluble in certain organic solvents, such as ether and chloroform. Lipids include a variety of compounds—fats, phospholipids, and steroids—that have vital functions in cells. The most abundant lipids are fats.

**Fats** are used primarily to store energy for cellular activities. Fat molecules can supply more energy, gram for gram, than carbohydrate molecules.

Like carbohydrates, fat molecules are composed of carbon, hydrogen, and oxygen atoms. However, fats have a much smaller proportion of oxygen atoms than do carbohydrates. The formula for the fat tristearin, $C_{57}H_{110}O_6$, illustrates these characteristic proportions.



**(a)** Some glucose molecules ($C_6H_{12}O_6$) have a straight chain of carbon atoms.

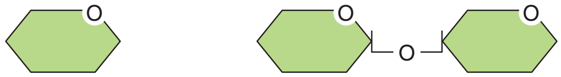
**(b)** More commonly, glucose molecules form a ring structure.

**(c)** This shape symbolizes the ring structure of a glucose molecule.

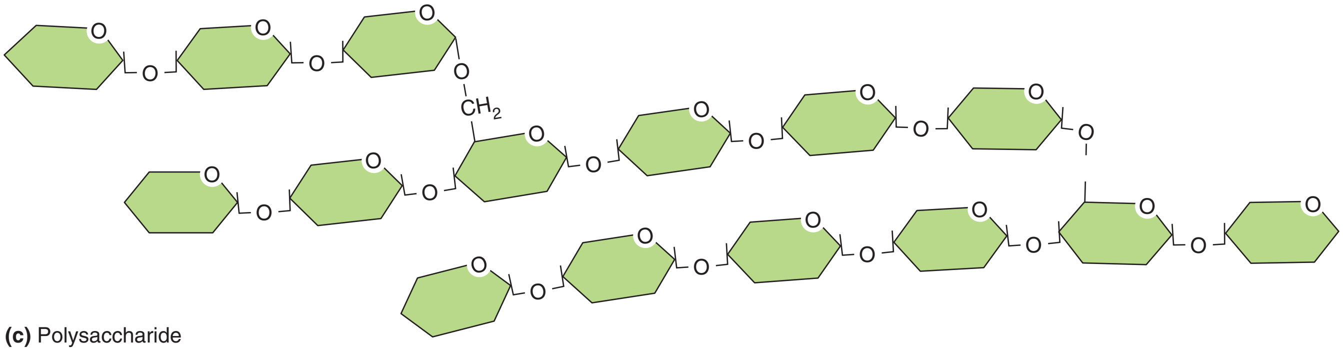
**FIGURE 2.12** Structural formulas depict a molecule of glucose.

The building blocks of fat molecules are **fatty acids** and **glycerol** (glis′er-ol). Each glycerol molecule bonds with three fatty acid molecules to produce a single fat, or *triglyceride,* molecule (fig. 2.14).

The glycerol portions of all fat molecules are identical, but fats are diverse because there are many kinds of fatty acids. Fatty acid molecules differ in the lengths of their carbon atom chains, which usually have an even number of carbon atoms. The chains also vary in the way the carbon atoms bond. In some molecules, the carbon atoms all join by single carbon-carbon bonds. This type of fatty acid is *saturated;* that is, each carbon atom is bound to as many hydrogen atoms as possible and is thus saturated with hydrogen atoms. Other fatty acid chains are not bound to the maximum number of hydrogen atoms. These fatty acids, therefore, have one



**(a)** Monosaccharide **(b)** Disaccharide



**(c)** Polysaccharide

**FIGURE 2.13** Carbohydrate molecules vary in size. **(a)** A monosaccharide molecule consists of one building block with 6 carbon atoms. **(b)** A disaccharide molecule consists of two of these building blocks. **(c)** A polysaccharide molecule consists of many such building blocks.

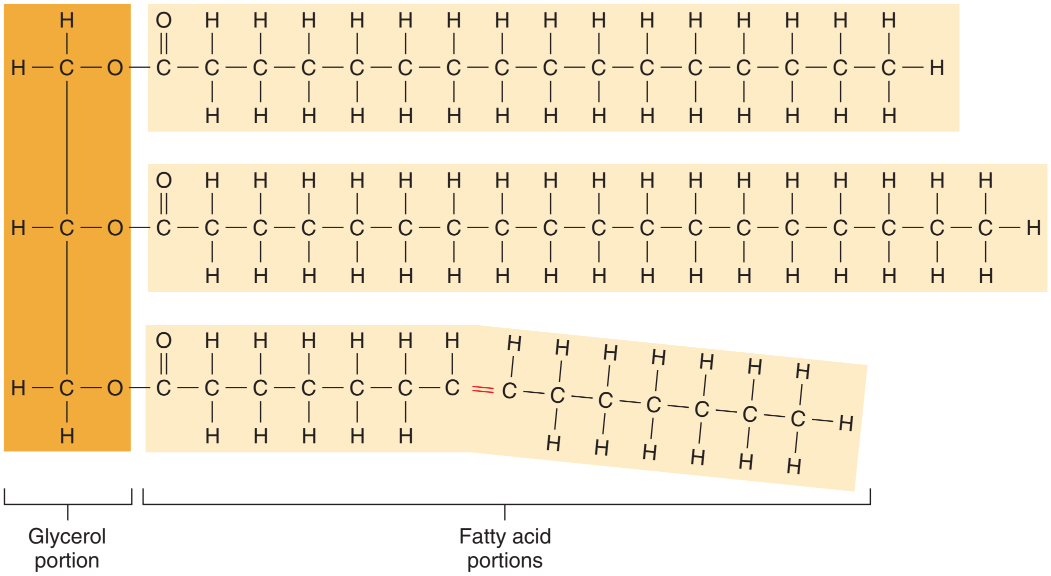


**FIGURE 2.14** A triglyceride molecule (fat) consists of a glycerol portion and three fatty acid portions. This is an example of an unsaturated fat. The double bond between carbon atoms in the unsaturated fatty acid is shown in red.

**Q** *Why is it incorrect to say that fat is another word for lipid?*

**Answer can be found in Appendix F on page 582.**

or more double bonds between carbon atoms, because a carbon atom must form four bonds to be stable. Fatty acid molecules with double bonds are *unsaturated,* and those with many double-bonded carbon atoms are *polyunsaturated.* Similarly, fat molecules that contain only saturated fatty acids are called *saturated fats,* and those that include unsaturated fatty acids are called *unsaturated fats.* The triglyceride molecule in figure 2.14 is an example of an unsaturated fat.

A **phospholipid** (fos″fo-lip′id) molecule is similar to a fat molecule in that it consists of a glycerol portion and fatty acid chains (fig. 2.15*a,b*). A phospholipid, however, has only two fatty acid chains; in place of the third is a portion that includes a phosphate group. The phosphate portion is soluble in water (hydrophilic) and forms the "head" of the molecule, whereas the fatty acid portion is insoluble in water (hydrophobic) and forms a "tail" (fig. 2.15*c*). Phospholipids are important in cellular structures.

**Steroid** (ste′roid) molecules are complex structures that include four connected rings of carbon atoms (fig. 2.16). Among the more important steroids are cholesterol, which is in all body cells and is used to synthesize other steroids: hormones such as estrogen and progesterone from the ovaries, testosterone from the testes; and several hormones from the adrenal glands. Chapters 11 and 19 discuss these steroids. Table 2.5 lists the three important groups of lipids and their characteristics.

**TABLE 2.5** Important Groups of Lipids

| Group | Basic Molecular Structure | Characteristics |
|---|---|---|
| Triglycerides | Three fatty acid molecules bound to a glycerol molecule | Most common lipids in body; stored in fat tissue as an energy supply; fat tissue also provides insulation beneath the skin |
| Phospholipids | Two fatty acid molecules and a phosphate group bound to a glycerol molecule | Used as structural components in cell membranes; abundant in liver and parts of the nervous system |
| Steroids | Four connected rings of carbon atoms | Widely distributed in the body and have a variety of functions; include cholesterol, hormones of adrenal cortex, hormones from the ovaries and testes, bile acids, and vitamin D |

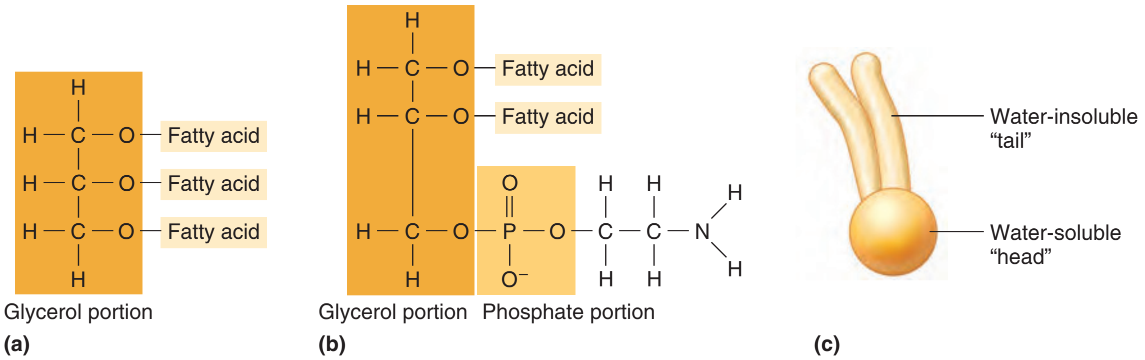
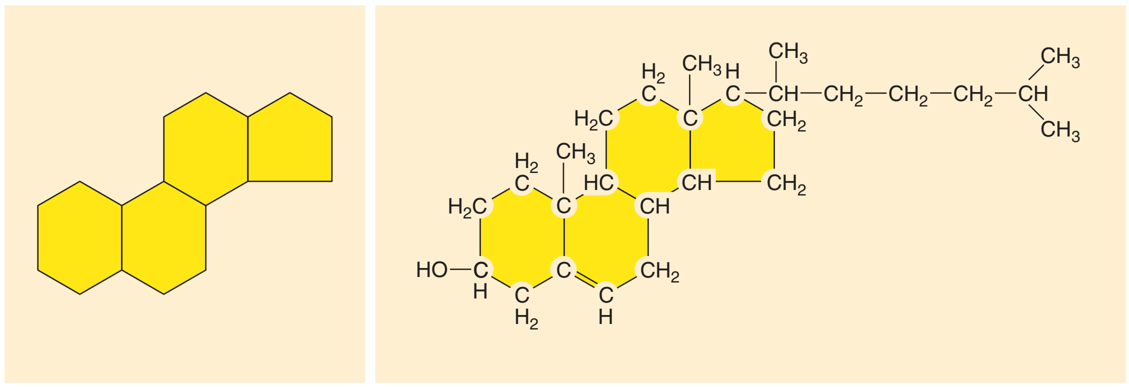


**FIGURE 2.15** Fats and phospholipids. **(a)** A fat molecule (triglyceride) consists of a glycerol and three fatty acids. **(b)** In a phospholipid molecule, a phosphate-containing group replaces one fatty acid. The unshaded portion may vary. **(c)** Schematic representation of a phospholipid.



**(a)** General structure of a steroid

**(b)** Cholesterol

**FIGURE 2.16** Steroid structure. **(a)** The general structure of a steroid. **(b)** The structural formula for cholesterol, a steroid widely distributed in the body.

Saturated fats are more abundant in fatty foods that are solids at room temperature, such as butter, lard, and most animal fats. Unsaturated fats are in foods that are liquid at room temperature, such as soft margarine and seed oils (corn, grape, sesame, soybean, sunflower, and peanut). Coconut and palm kernel oils are unusual in that they are high in saturated fats but are liquids at room temperature. The most heart-healthy fats are olive and canola (rapeseed) oils, which are monounsaturated—that is, they have one carbon-carbon double bond.

Manufacturers add hydrogen atoms to certain vegetable oils to make them harder and easier to use. This process, called hydrogenation, produces fats that are partially unsaturated and also "trans." ("Trans" refers to atoms in a molecule on opposite sides of a backbone-like structure, like stores on opposite sides of a street. Atoms on the same side—like stores on the same side of a street—are called "cis.")

### *Proteins*

**Proteins** (pro′tēnz) have a variety of functions in the body. Many serve as structural materials, energy sources, or hormones. Some proteins combine with carbohydrates (to form glycoproteins) and function as receptors on cell surfaces, allowing cells to respond to specific types of molecules that bind to them. Proteins called *antibodies* detect and destroy foreign substances in the body. Metabolism could not occur fast enough to support life were it not for proteins called *enzymes,* which catalyze specific chemical reactions. (Enzymes are discussed in more detail in chapter 4, pp. 88–89.)

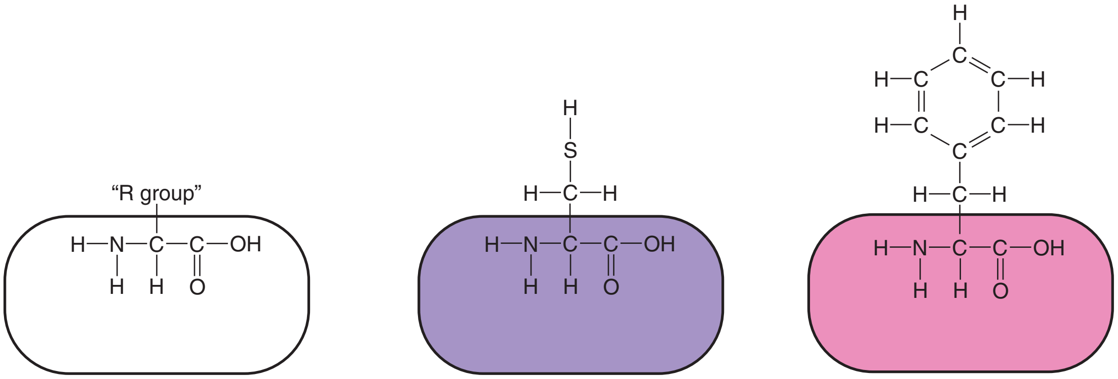
Like carbohydrates and lipids, proteins are composed of atoms of carbon, hydrogen, and oxygen. In addition, all proteins contain nitrogen atoms, and some contain sulfur atoms. The building blocks of proteins are **amino acids,** each of which has an *amino group* (—$NH_2$) at one end and a *carboxyl group* (—COOH) at the other (fig. 2.17*a*). Amino acids also have a *side chain,* or *R group* ("R" may be thought of as the "rest of the molecule"). The composition of the R group distinguishes one type of amino acid from another (fig. 2.17*b*).

Twenty different types of amino acids make up the proteins of most living organisms. The amino acids join in polypeptide chains that vary in length from less than 100 to more than 5,000 amino acids. A protein molecule consists of one or more polypeptide chains.

A human body has more than 200,000 types of proteins, but only about 20,500 genes, which are the instructions for production of particular polypeptides. The numbers are not the same because parts of some genes encode sequences of amino acids found in more than one type of protein. It is a little like assembling a large and diverse wardrobe from a few basic pieces of clothing.

Proteins have several levels of structure, shown in figure 2.18*a–c*. Primary structure is the amino acid sequence. Secondary structure results from attractions between amino acids that are close together in the amino acid sequence. Tertiary structure introduces folds due to attractions between amino acids far apart in the amino acid sequence.

Hydrogen bonding and covalent bonding between atoms in different parts of the polypeptide give the final protein a distinctive three-dimensional shape, or **conformation** (fig. 2.19). The conformation of a protein determines its function. Some proteins are long and fibrous, such as the keratin proteins that form hair, or fibrin, the protein whose threads form a blood clot. Many proteins are globular and function as enzymes,

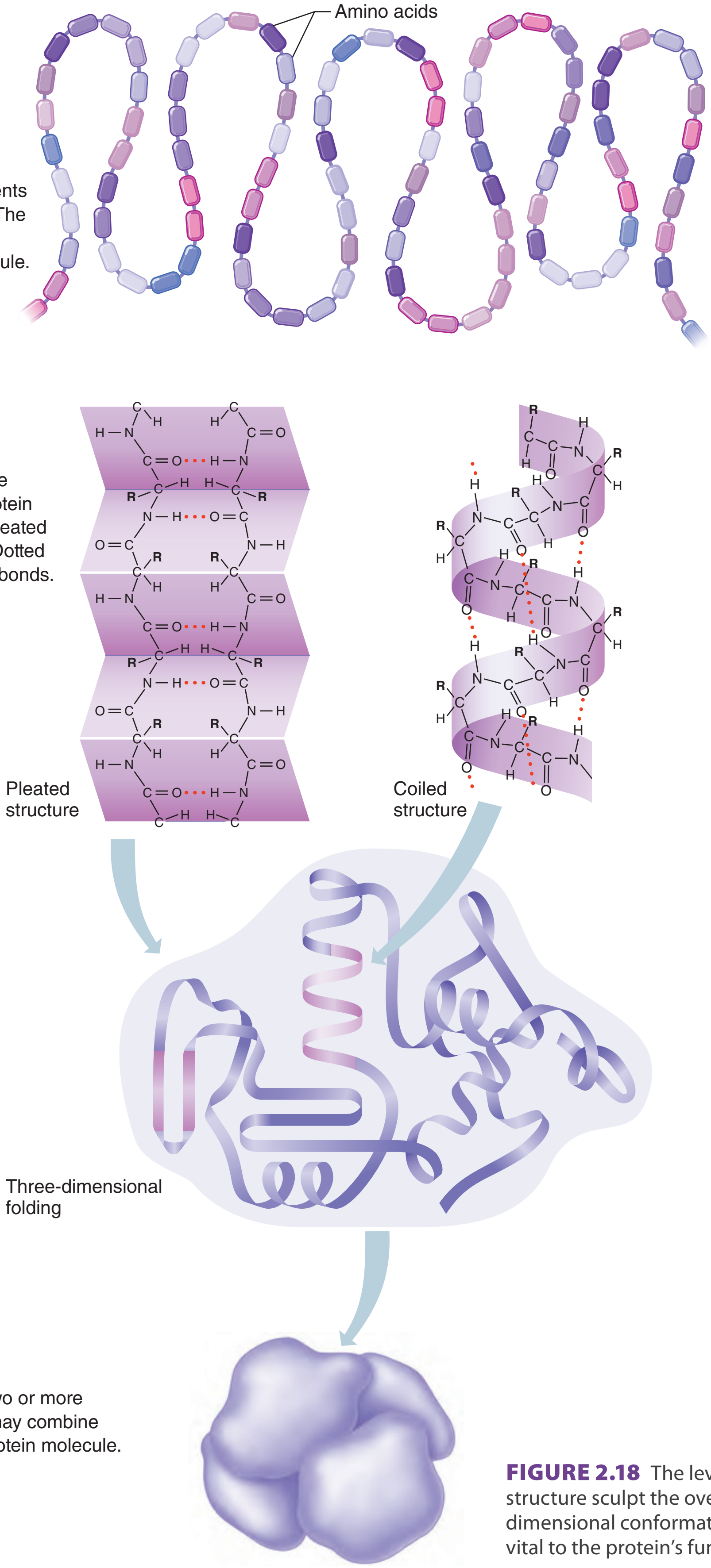


**(a)** General structure of an amino acid. The portion common to all amino acids is within the oval. It includes the amino group (—$NH_2$) and the carboxyl group (—COOH). The "R group", or the "rest of the molecule," varies and is what makes each type of amino acid unique.

**(b)** Cysteine. Cysteine has an R group that contains sulfur.

Phenylalanine. Phenylalanine has a complex R group.

**FIGURE 2.17** Amino acid structure. **(a)** An amino acid has an amino group, a carboxyl group, and a hydrogen atom that are common to all amino acid molecules, and a specific R group. **(b)** Some representative amino acids and their structural formulas. Each type of amino acid molecule has a particular shape due to its R group.



**(a)** Primary structure—Each oblong shape in this polypeptide chain represents an amino acid molecule. The whole chain represents a portion of a protein molecule.

**(b)** Secondary structure—The polypeptide chain of a protein molecule is often either pleated or twisted to form a coil. Dotted lines represent hydrogen bonds. R groups (see fig. 2.17) are indicated in bold.

**(c)** Tertiary structure—The pleated and coiled polypeptide chain of a protein molecule folds into a unique three-dimensional structure.

**(d)** Quaternary structure—Two or more proteins, often different, may combine to form a single, larger protein molecule.

**FIGURE 2.18** The levels of protein structure sculpt the overall, three-dimensional conformation, which is vital to the protein's function.

ion channels, carrier proteins, or receptors. Myoglobin and hemoglobin, which transport oxygen in muscle and blood, respectively, are globular.

For some proteins, slight, reversible changes in conformation are part of their normal function. For example, some of the proteins involved in muscle contraction exert a pulling force as a result of such a shape change, leading to movement. The reversibility of these changes enables the protein to function repeatedly.

When hydrogen bonds in a protein break as a result of exposure to excessive heat, radiation, electricity, pH changes, or certain chemicals, a protein's unique shape may be changed dramatically, or *denatured.* Such proteins lose their special properties. For example, heat denatures the protein in egg white (albumin), changing it from a liquid to a solid. This is an irreversible change—a hard-boiled egg cannot return to its uncooked, runny state. Similarly, cellular proteins that are denatured may be permanently altered and lose their functions.

Proteins with more than one polypeptide chain have a fourth level of conformation, the *quaternary structure.* The constituent polypeptides are connected, forming a very large protein (see fig. 2.18*d*). Hemoglobin is a quaternary protein made up of four separate polypeptide chains.

For most proteins, the conformation, which determines its function, is always the same for a given amino acid sequence or primary structure. Thus, it is the amino acid sequence that ultimately determines the role of a protein in the body. Genes, made of the nucleic acid DNA, contain the information for the amino acid sequences of all the body's proteins in a form that the cell can decode.

**FIGURE 2.19** A model of a portion of the protein collagen. The complex shape of a protein is characteristic of that protein and determines its functional properties.

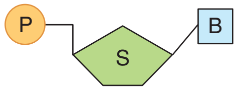


**FIGURE 2.20** A nucleotide consists of a 5-carbon sugar (S = sugar), a phosphate group (P = phosphate), and a nitrogenous base (B = base).

### Nucleic Acids

**Nucleic acids** (nu-kle′ik as′idz) form genes and take part in protein synthesis. These molecules are generally very large. They include atoms of carbon, hydrogen, oxygen, nitrogen, and phosphorus, which form building blocks called **nucleotides.** Each nucleotide consists of a 5-carbon *sugar* (ribose or deoxyribose), a *phosphate group,* and one of several *nitrogenous* (nitrogen-containing) *bases* (fig. 2.20). A nucleic acid molecule consists of a chain of many nucleotides (polynucleotide chain).

Nucleic acids are of two types. One type—**RNA (ribonucleic acid)** (ri″bo-nu-kle′ik as′id)—is composed of molecules whose nucleotides have ribose. Most RNA molecules are single-stranded polynucleotide chains, but they can fold into shapes that enable them to interact with DNA (fig. 2.21*a*). The second type of nucleic acid—**DNA (deoxyribonucleic acid)** (de-ok′si-ri″bo-nu-kle″ik as′id)—has deoxyribose and forms a double polynucleotide chain. The two chains are held together by hydrogen bonds (fig. 2.21*b*).

DNA molecules store information in a type of molecular code created by the sequences of the four types of nitrogenous bases. Cells use this information to synthesize protein molecules. RNA molecules carry out protein synthesis. (Nucleic acids are discussed in more detail in chapter 4, pp. 94–99.) Certain nucleotides, such as adenosine triphosphate (ATP), have another role providing energy to chemical reactions (fig. 2.22). ATP is discussed further in chapter 4 (p. 91).

Table 2.6 summarizes the four groups of organic compounds. Clinical Application 2.2 discusses the use of biomarkers (both organic and inorganic compounds) in disease diagnosis, indicators of toxin exposure, and forensics.

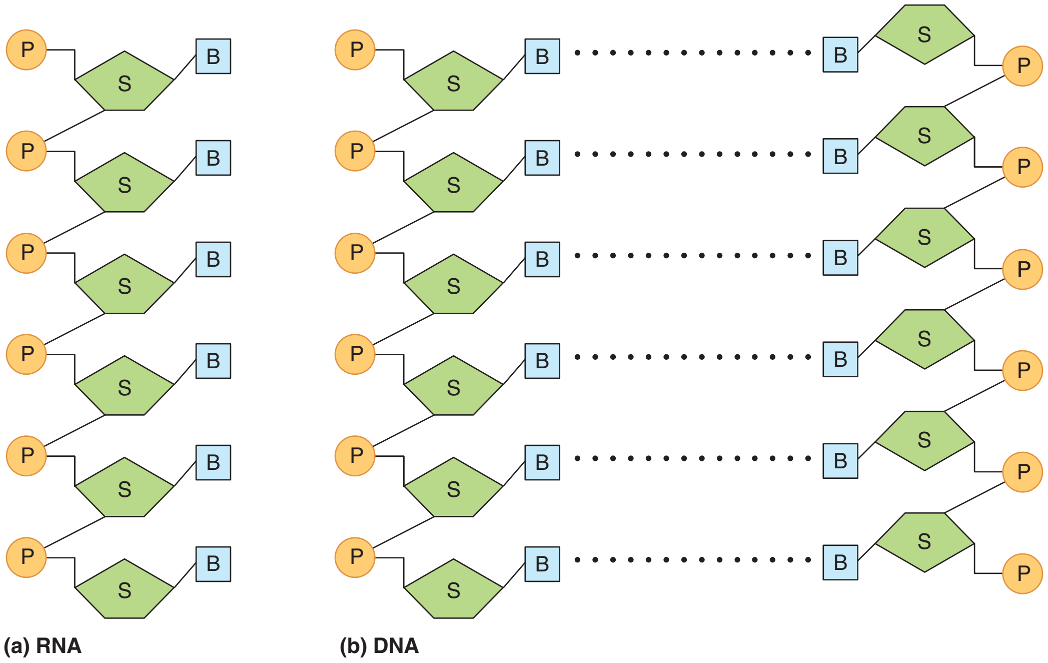


**FIGURE 2.21** A schematic representation of nucleic acid structure. A nucleic acid molecule consists of **(a)** one (RNA) or **(b)** two (DNA) polynucleotide chains. DNA chains are held together by hydrogen bonds (dotted lines), and they entwine, forming a double helix.

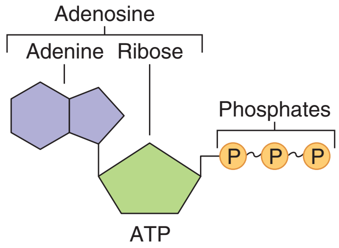


**FIGURE 2.22** An ATP (adenosine triphosphate) molecule consists of an adenine, a ribose, and three phosphates. The wavy lines connecting the last two phosphates represent high-energy chemical bonds. When broken, these bonds release energy, which the cell uses for metabolic processes.

**TABLE 2.6** **Organic Compounds in Cells**

| Compound | Elements Present | Building Blocks | Functions | Examples |
|---|---|---|---|---|
| Carbohydrates | C,H,O | Simple sugars | Provide energy, cell structure | Glucose, starch |
| Lipids | C,H,O (often P) | Glycerol, fatty acids, phosphate groups | Provide energy, cell structure | Triglycerides, phospholipids, steroids |
| Proteins | C,H,O,N (often S) | Amino acids | Provide cell structure, enzymes, energy | Albumins, hemoglobin |
| Nucleic acids | C,H,O,N,P | Nucleotides | Store information for protein synthesis; control cell activities | RNA, DNA |

Recall that water molecules are polar. Many larger molecules, including carbohydrates, proteins, and nucleic acids, have polar regions and dissolve easily in water as a result. Unlike electrolytes, however, these molecules do not dissociate when they dissolve in water—they remain intact. Such water-soluble molecules are said to be hydrophilic (they "like" water).

Molecules that lack polar regions, such as triglycerides and steroids, do not dissolve in water ("oil and water don't mix"). Such molecules do dissolve in lipid and are said to be lipophilic (they "like" lipid).

Water solubility and lipid solubility are important factors in drug delivery and in the movement of substances throughout the body. Much of this is discussed further in chapter 3 (pp. 62–64).

## PRACTICE

17. Compare the chemical composition of carbohydrates, lipids, proteins, and nucleic acids.
18. How does an enzyme affect a chemical reaction?
19. What is the chemical basis of the great diversity of proteins?
20. What are the functions of nucleic acids?

## CLINICAL APPLICATION 2.2

## Biomarkers

A biomarker is a chemical in the body that indicates a disease process or exposure to a toxin. Tests that measure levels of specific biomarkers may be used to indicate increased risk of developing a particular disease, to help diagnose a disease, or to select a treatment.

A familiar biomarker is the level of low-density lipoprotein (LDL) in blood serum. LDL is one of five sizes of lipoproteins that carry cholesterol and other lipids. Elevated LDL indicates increased risk of developing heart and blood vessel disease. Considered along with other factors such as family history, the biomarker test results may lead a physician to prescribe an LDL-lowering drug.

A clinical test based on a biomarker must meet certain criteria. Practical considerations include how easy the biomarker is to obtain and measure, and the cost of the biomarker test compared to the cost for treating disease detected at a more advanced stage. A blood or urine test, for example, is a simple way to sample a biomarker. Sensitivity and specificity are also important criteria for biomarkers. Sensitivity is the ability to detect disease only when it is actually present. Specificity is the biomarker test's ability to exclude the disease in a patient who does not actually have it.

A biomarker must also have the same predictive power in different individuals. For example, C-reactive protein is produced in response to inflammation, and high-density lipoproteins (HDLs) are large cholesterol-carrying particles. Both were once considered biomarkers for coronary heart disease, but recently researchers discovered that they are predictive only in people with certain genetic backgrounds.

Tests that include several biomarkers provide more information than single biomarker tests. For example, to assess exposure to tobacco smoke, a biomarker panel measures carbon monoxide and biochemicals that the body produces as it breaks down carcinogens in cigarette smoke. Biomarker panels are also valuable in selecting drugs most likely to work to treat a specific subtype of cancer in a particular individual.

## Summary Outline

### 2.1 Introduction (p. 40)

*Chemistry describes the composition of substances and how chemicals react with each other. The human body is composed of chemicals.*

### 2.2 Structure of Matter (p. 40)

1. Elements and atoms
   a. Matter is composed of elements.
   b. Some elements occur in pure form, but many are found combined with other elements.
   c. Elements are composed of atoms, which are the smallest complete units of elements.
   d. Atoms of different elements have characteristic sizes, weights,and ways of interacting.
2. Atomic structure
   a. An atom consists of one or more electrons surrounding a nucleus, which contains one or more protons and usually one or more neutrons.
   b. Electrons are negatively charged, protons are positively charged, and neutrons are uncharged.
   c. A complete atom is electrically neutral.
   d. An element's atomic number is equal to the number of protons in each atom. The atomic weight is equal to the number of protons plus the number of neutrons in each atom.
   e. Isotopes are atoms with the same atomic number but different atomic weights.
   f. Some isotopes are radioactive.
3. Bonding of atoms
   a. When atoms combine, they gain, lose, or share electrons.
   b. Electrons occupy shells around a nucleus.
   c. Atoms with completely filled outer shells are inert, but atoms with incompletely filled outer shells tend to gain, lose, or share electrons and thus achieve stable structures.
   d. Atoms that lose electrons become positively charged ions. Atoms that gain electrons become negatively charged ions.
   e. Ions with opposite electrical charges attract and form ionic bonds. Atoms that share electrons form covalent bonds.
   f. A polar covalently bonded molecule has an uneven distribution of charges.
   g. The attraction of the positive hydrogen end of a polar molecule to the negative nitrogen or oxygen end of another polar molecule is called a hydrogen bond.
4. Molecules and compounds
   a. Two or more atoms of the same element may bond to form a molecule of that element. Atoms of different elements may bond to form a molecule of a compound.
   b. Molecules consist of definite kinds and numbers of atoms.
5. Formulas
   a. A molecular formula represents the numbers and types of atoms in a molecule.
   b. A structural formula depicts the arrangement of atoms within a molecule.
6. Chemical reactions
   a. A chemical reaction breaks or forms bonds between atoms, ions, or molecules.
   b. Three types of chemical reactions are: synthesis, in which larger molecules form from smaller particles; decomposition, in which larger molecules are broken down into smaller particles; and exchange reactions, in which the parts of two different molecules trade positions.

    c. Many reactions are reversible. The direction of a reaction depends on the proportions of reactants and end products, the energy available, and the presence of catalysts.
  7. Acids and bases
    a. Compounds that release ions in water are electrolytes.
    b. Electrolytes that release hydrogen ions are acids, and those that release hydroxide or other ions that react with hydrogen ions are bases.
    c. A value called pH represents a solution's concentration of hydrogen ions ($H^+$) and hydroxide ions ($OH^-$).
    d. A solution with equal numbers of $H^+$ and $OH^-$ is neutral and has a pH of 7.0. A solution with more $H^+$ than $OH^-$ is acidic and has a pH less than 7.0. A solution with fewer $H^+$ than $OH^-$ is basic and has a pH greater than 7.0.
    e. Each whole number on the pH scale represents a tenfold difference in the hydrogen ion concentration.
    f. Buffers are chemicals that resist pH change.
    g. The pH in the internal environment is regulated.

**2.3 Chemical Constituents of Cells (p. 49)**

*Molecules that have carbon and hydrogen atoms are organic and are usually nonelectrolytes. Other molecules are inorganic and are usually electrolytes.*

1. Inorganic substances
    a. Water is the most abundant compound in the body and is a solvent in which chemical reactions occur. Water transports chemicals and heat.
    b. Oxygen releases energy from glucose and other nutrients. This energy drives metabolism.
    c. Carbon dioxide is produced when metabolism releases energy.
    d. Salts provide a variety of ions that metabolic processes require.
2. Organic substances
    a. Carbohydrates provide much of the energy that cells require and also contribute to cell structure. Their basic building blocks are simple sugar molecules.
    b. Lipids, such as fats, phospholipids, and steroids, supply energy and build cell parts. The basic building blocks of fats are molecules of glycerol and fatty acids.
    c. Proteins serve as structural materials, energy sources, hormones, cell surface receptors, and enzymes.
        (1) The building blocks of proteins are amino acids.
        (2) Proteins vary in the numbers, types, and sequences of their amino acids.
        (3) Primary structure is the amino acid sequence. Secondary structure comes from attractions between amino acids that are close together in the primary structure. Tertiary structure reflects attractions of far-apart amino acids and folds the molecule.
        (4) The amino acid chain of a protein molecule folds into a complex shape (conformation) that is maintained largely by hydrogen bonds.
        (5) Excessive heat, radiation, electricity, altered pH, or various chemicals can denature proteins.
    d. Nucleic acids are the genetic material and control cellular activities.
        (1) Nucleic acid molecules are composed of nucleotides.
        (2) The two types of nucleic acids are RNA and DNA.
        (3) DNA molecules store information that cell parts use to construct specific protein molecules. RNA molecules help synthesize proteins.

## CHAPTER ASSESSMENTS

### 2.1 Introduction

**1.** Define *chemistry.* (p. 40)

### 2.2 Structure of Matter

**2.** Define *matter.* (p. 40)
**3.** Explain the relationship between elements and atoms. (p. 40)
**4.** List the four most abundant elements in the human body. (p. 40)
**5.** Describe the parts of an atom and where they are found within the atom. (p. 41)
**6.** Explain why a complete atom is electrically neutral. (p. 41)
**7.** Define *atomic number, atomic weight,* and *isotope.* (p. 41)
**8.** Explain how electrons are distributed within the electron shells of an atom. (p. 42)
**9.** An ionic bond forms when ________ . (p. 44)
  a. atoms share electrons
  b. positively charged and negatively charged parts of polar covalent molecules attract
  c. ions with opposite electrical charges attract
  d. two atoms exchange protons
**10.** Explain the relationship between molecules and compounds. (p. 45)
**11.** Show the difference between a molecular formula and a structural formula. (p. 46)
**12.** The formula $C_6H_{12}O_6$ means ________. (p. 46)
**13.** Three major types of chemical reactions are ________ , ________ , and ________. (p. 47)
**14.** Explain what a reversible reaction is. (p. 47)
**15.** Define *catalyst.* (p. 47)
**16.** Define *acid* and *base.* (p. 47)
**17.** Explain what pH measures, and describe the pH scale. (p. 48)
**18.** Define *buffer.* (p. 48)

### 2.3 Chemical Constituents of Cells

**19.** Distinguish between inorganic and organic substances. (p. 49)
**20.** Distinguish between electrolytes and nonelectrolytes. (p. 49)
**21.** Describe the roles water and oxygen play in the human body. (p. 49)
**22.** List several ions in body fluids. (p. 49)
**23.** Describe the general characteristics of carbohydrates. (p. 49)
**24.** Distinguish between simple sugars and complex carbohydrates. (p. 49)
**25.** Describe the general characteristics of lipids, and list the three main kinds of lipids. (p. 50)
**26.** A triglyceride molecule consists of ______________ . (p. 51)
  a. 3 fatty acids and 1 glycerol
  b. 3 monosaccharides
  c. 3 amino acids
  d. 3 glycerols and 1 fatty acid
**27.** Explain the difference between saturated and unsaturated fats. (p. 52)

**28.** A hydrophilic molecule dissolves in ________. (p. 52)
   a. lipid but not water
   b. water but not lipid
   c. neither lipid nor water
   d. both lipid and water

**29.** List at least three functions of proteins. (p. 53)
**30.** Describe four levels of protein structure. (p. 53)
**31.** Explain how protein molecules may denature. (p. 55)
**32.** Describe the structure of nucleic acids. (p. 55)
**33.** Explain the major functions of nucleic acids. (p. 55)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOME 2.2

1. An advertisement for a cosmetic powder claims that the product is "chemical-free." Explain why this is impossible.
2. The thyroid gland metabolizes iodine, the most common form of which has a molecular weight of 127 ($^{127}$I). A physician wants to use a radioactive isotope of iodine ($^{123}$I) to test whether a patient's thyroid gland is metabolizing normally. Based on what you know about how atoms react, do you think this physician's plan makes sense or not?

### OUTCOMES 2.2, 2.3

3. What acidic and basic substances do you encounter in your everyday activities? What acidic foods do you eat regularly? What basic foods do you eat?

### OUTCOME 2.3

4. A topping for ice cream contains fructose, hydrogenated soybean oil, salt, and cellulose. What types of chemicals are in it?
5. At a restaurant, a waiter recommends a sparkling carbonated beverage, claiming that it contains no carbohydrates. The product label lists water and fructose as ingredients. Is the waiter correct?
6. How would you explain the dietary importance of amino acids and proteins to a person who is following a diet composed primarily of carbohydrates?
7. A friend, while frying some eggs, points to the change in the egg white (which contains a protein called albumin) and explains that if the conformation of a protein changes, it will no longer have the same properties and will lose its ability to function. Do you agree or disagree with this statement?

## ONLINE STUDY TOOLS www.mhhe.com/shieress12

LEARN PRACTICE ASSESS

**Connect Interactive Questions** Reinforce your knowledge using assigned interactive questions covering atomic structure, and inorganic and organic substances.

**Connect Integrated Activity** Maintaining pH is important to homeostasis. How well do you understand acids, bases, and buffers?

**LearnSmart** Discover which chapter concepts you have mastered and which require more attention. This adaptive learning tool is personalized, proven, and preferred.

**Anatomy & Physiology Revealed** View animations on atomic structure, chemical bonds, and electrolytes.

# 3

# Cells

*Neurons do not divide and are therefore difficult to use in culture to study a disease process (400x). Researchers can study them by using a technique called cellular reprogramming, which stimulates one cell type to divide and give rise to another cell type.*

**Reprogramming a cell.** The first signs of amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, are subtle—a foot drags, clothing feels heavy on the body, or an exercise usually done with ease becomes difficult. An actor was fired from a starring television role because of his slurred speech, and a teacher retired when he could no longer hold chalk or pens. Usually within five years of noticing these first signs, failure of the motor neurons that stimulate muscles becomes so widespread that breathing unaided becomes impossible.

ALS currently has no treatment. Part of the reason is that because neurons do not divide, they cannot reveal the changes that occur with the disease when grown in laboratory culture for researchers. A new technology called cellular reprogramming, however, can take a specialized cell type back to a stage at which it can specialize in any of several ways. Then, by adding certain chemical factors, researchers can guide the specialization toward the cell type that is affected in a certain disease. Cells can be reinvented in this way because they all contain a complete set of genes. Such a reprogrammed cell is like a stem cell, but it does not come from an embryo—and it grows in a lab dish.

For ALS, cells taken from arm skin of two women in their eighties who have mild cases were reprogrammed to specialize as motor neurons. Researchers can now observe the very first inklings of the disease and use the findings to identify new drug targets and develop new drugs.

ALS was the first of hundreds of diseases now represented by reprogrammed cells, including inherited immune deficiencies, diabetes, blood disorders, and Parkinson's disease. In the future, reprogrammed cells might be used therapeutically to replace abnormal cells. First, though, researchers must learn how to control the integration of reprogrammed cells into tissues and organs in the body.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 3.1 Introduction

1. Explain how cells differ from one another. (p. 61)

### 3.2 Composite Cell

2. Explain how the structure of a cell membrane makes possible its functions. (p. 62)
3. Describe each type of organelle, and explain its function. (pp. 65–69)
4. Describe the cell nucleus and its parts. (pp. 69–70)

### 3.3 Movements Through Cell Membranes

5. Explain how substances move into and out of cells. (pp. 70–77)

### 3.4 The Cell Cycle

6. Explain why regulation of the cell cycle is important to health. (p. 77)
7. Describe the cell cycle. (p. 77)
8. Explain how stem cells and progenitor cells make possible growth and repair of tissues. (pp. 80–82)
9. Explain how two differentiated cell types can have the same genetic information, but different appearances and functions. (pp. 80–82)

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## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**cyt-** [cell] *cyt*oplasm: Fluid (cytosol) and organelles that occupy the space between the cell membrane and the nuclear envelope.

**endo-** [within] *endo*plasmic reticulum: Complex of membranous structures within the cytoplasm.

**hyper-** [above] *hyper*tonic: Solution that has a greater osmotic pressure than body fluids.

**hypo-** [below] *hypo*tonic: Solution that has a lesser osmotic pressure than body fluids.

**inter-** [between] *inter*phase: Stage between the end of one cell division and the beginning of the next.

**iso-** [equal] *iso*tonic: Solution that has the same osmotic pressure as body fluids.

**mit-** [thread] *mit*osis: Process of cell division when threadlike chromosomes become visible within a cell.

**phag-** [to eat] *phag*ocytosis: Process by which a cell takes in solid particles.

**pino-** [to drink] *pino*cytosis: Process by which a cell takes in tiny droplets of liquid.

**-som** [body] ribo*som*e: Tiny, spherical structure that consists of protein and RNA and functions in protein synthesis.

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## 3.1 | Introduction

A cell is the unit of life. It contains several types of structures that house the chemical reactions that make life possible. A human body has about 75 trillion cells. They connect and interact, forming dynamic tissues, organs, and organ systems.

The cells that make up an adult human body have similarities and distinctions. Cells consist of the same basic structures, yet vary considerably in the number and distribution of their component structures, and in size and shape. The three-dimensional forms of cells make possible their functions, as figure 3.1 illustrates. For instance, some nerve cells have long, threadlike extensions that conduct electrical impulses from one part of the body to another. Epithelial cells that line the inside of the mouth are thin, flattened, and tightly packed into a tile-like layer that protects cells beneath them. Muscle cells, which pull structures closer together, are slender and rodlike. The precise alignment of the protein fibers in muscle cells provides the strength to withstand the contraction that moves the structures to which they attach.

A cell continually carries out activities essential for life, as well as more specialized functions, and adapts to changing conditions. The genes control a cell's actions and responses. Nearly all cells have a complete set of genetic instructions (the genome), yet they use only some of this information. Like a person accessing only a small part of the Internet, a cell accesses only some of the vast store of information in the genome to survive and specialize.

## 3.2 | Composite Cell

Cells vary greatly in size, shape, content, and function, and therefore describing a "typical" cell is challenging. The cell shown in figure 3.2 and described in this chapter is a composite cell that includes many known cell structures. In reality, any given cell has most, but perhaps not all, of these structures, and cells have differing numbers of some of them.

Under the light microscope, a properly applied stain reveals three basic cell parts: the **cell membrane** (sel mem′-brān) that encloses the cell, the **nucleus** (nu′kle-us) that houses the genetic material and controls cellular activities, and the **cytoplasm** (si′to-plazm) that fills out the cell.

Within the cytoplasm are specialized structures called **organelles** (or-gan-elz′), which can be seen clearly only under the higher magnification of electron

### CAREER CORNER

### Cytotechnologist

The woman has been tired for months, but blames it on frequent respiratory infections. When she notices several bruises, she visits her primary care physician, who sends a sample of her blood to a laboratory for analysis.

The cytotechnologist who prepares a microscope slide from the blood sample and examines it finds that there are too many white blood cells and too few red blood cells and platelets, and suspects that the patient has leukemia—a blood cancer.

A cytotechnologist recognizes signs of illness in cells. The job requires a bachelor's degree in biology, chemistry, or a related field that includes one to two years of an accredited program in cytotechnology. Further certification is available for Specialist in Cytotechnology and Technologist in Molecular Pathology, which may open up jobs in education and management. Cytotechnologists work independently but may consult with pathologists.

Cytotechnologists work in hospitals, doctors' offices, outpatient clinics, and diagnostic laboratories. Some tests performed on cells use automated equipment to identify cancerous or infected cells, but others require the cytotechnologist's judgment, based on experience with and knowledge of cell biology.

A career in cytotechnology can be very rewarding, because detecting disease on the cellular level is critical to accurate diagnosis of many conditions. Cytotechnologists can also work in research settings and selling laboratory equipment.

microscopes. Organelles are suspended in a liquid called *cytosol*. They are not static and still, as figure 3.2 might suggest. Some organelles move within the cell, and even those that appear not to move are the sites of ongoing biochemical activity. Organelles perform specific functions, such as partitioning off biochemicals that might harm other cell parts; dismantling debris; processing secretions; and extracting energy from nutrients. Organelles interact, creating vast networks.

## PRACTICE

1. Give three examples of how a cell's shape makes possible the cell's function.
2. Name the three major parts of a cell and their functions.
3. Define organelles and explain their general functions in a cell.

## Cell Membrane

The cell membrane (also called the *plasma membrane*) is more than a simple boundary holding in the cellular contents. It is an actively functioning part of the living material. The cell membrane regulates movement of substances in and out of the cell and is the site of much biological activity. Many of a cell's actions that enable it to survive and to interact with other cells use a molecular communication process called *signal transduction*. A series of molecules that are part of the cell membrane form pathways that detect signals from outside the cell and transmit them inward, where yet other molecules orchestrate the cell's response. The cell membrane also helps cells attach to certain other cells, which is important in forming tissues.

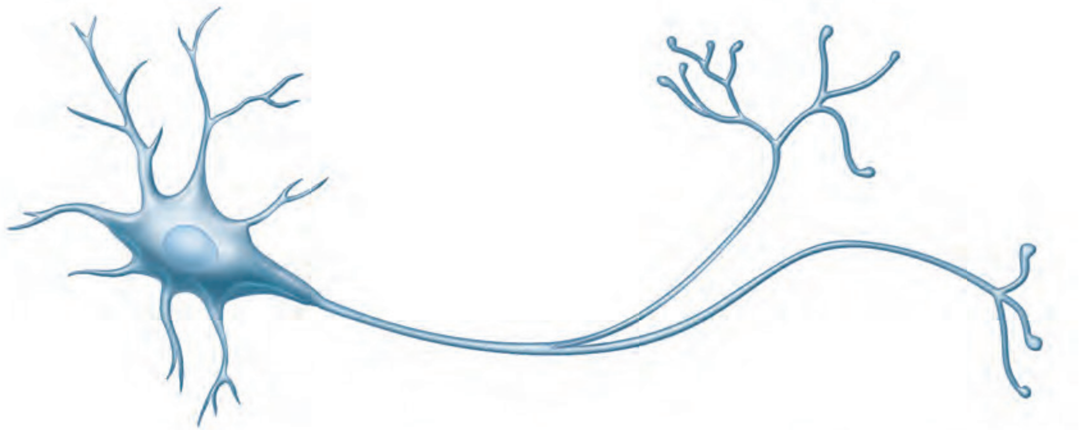
### General Characteristics

The cell membrane is extremely thin, flexible, and somewhat elastic. It typically has complex surface features with many outpouchings and infoldings that increase surface area (fig. 3.2). In addition to maintaining cell integrity, the cell membrane is **selectively permeable** (se-lek′tiv-le per′me-ah-bl) (also known as *semipermeable* or *differentially permeable*), which means that only certain substances can enter or leave the cell.

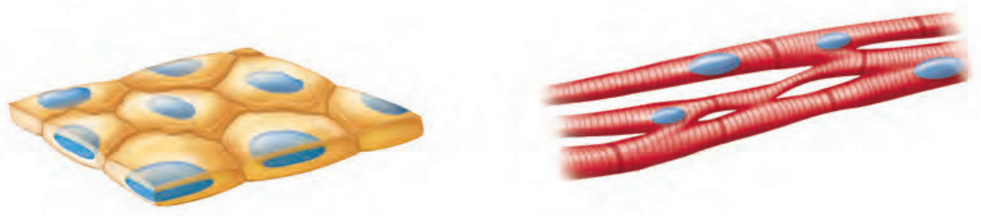
### Cell Membrane Structure

A cell membrane is composed mainly of lipids and proteins, with fewer carbohydrates (fig. 3.3). Its basic framework is a double layer, or *bilayer*, of phospholipid molecules (see fig. 3.2). Each phospholipid molecule includes a phosphate group and two fatty acids bound to a glycerol molecule (see chapter 2, p. 52). The water-soluble phosphate "heads" form the surfaces of the membrane, and the water-insoluble fatty acid "tails" make up the interior of the membrane. The lipid molecules can move sideways within the plane of the membrane. The two membrane layers form a soft and flexible, but stable, fluid film.

The cell membrane's interior is oily because it consists largely of the fatty acid tails of the phospholipid molecules.



**(a)** A nerve cell's long extensions enable it to conduct electrical impulses from one body part to another.

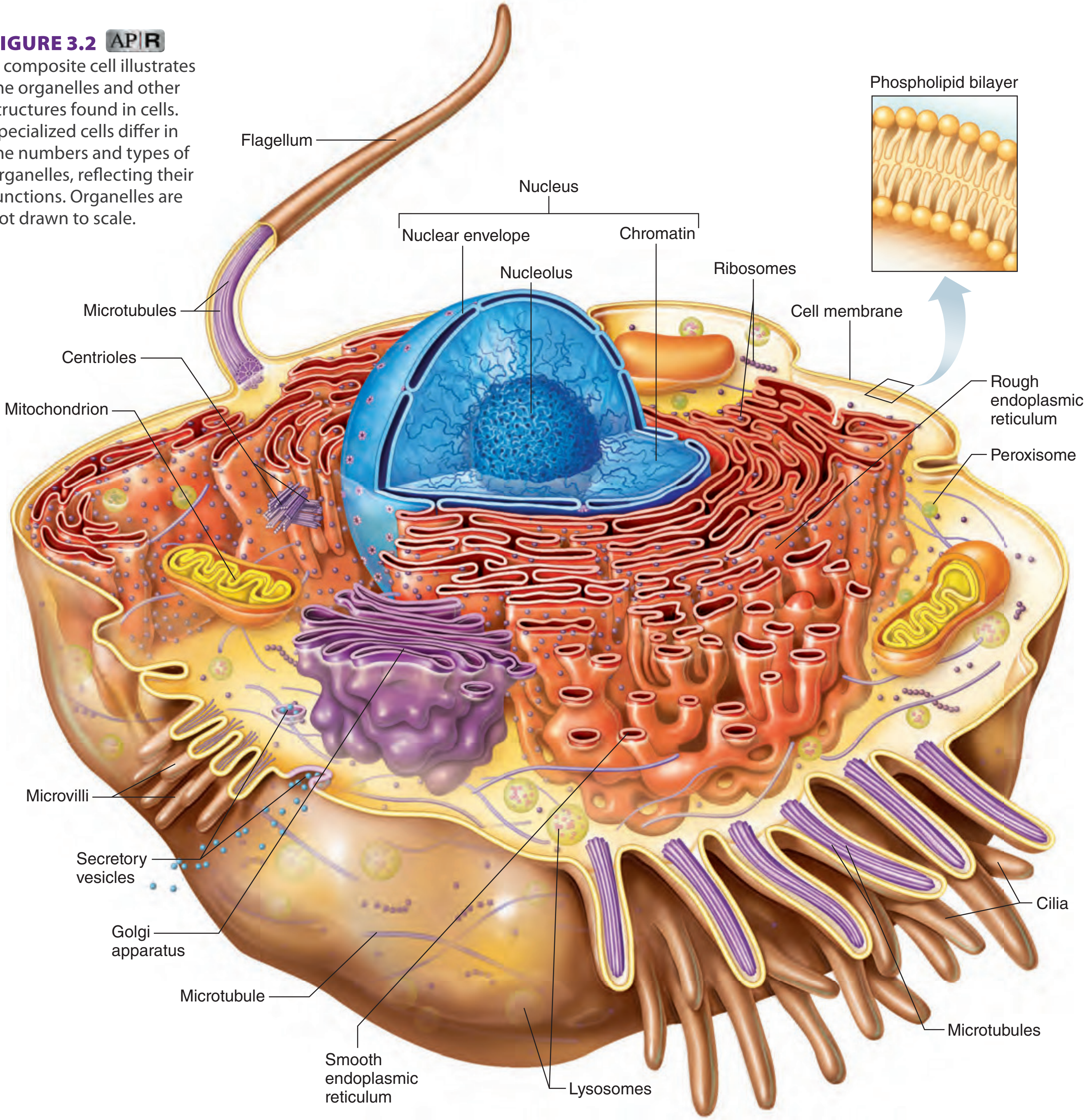


**(b)** The sheetlike organization of epithelial cells enables them to protect underlying cells.

**(c)** The alignment of contractile proteins within muscle cells enables them to contract, pulling closer together the structures to which they attach.

**FIGURE 3.1** Cells vary in structure and function.

**FIGURE 3.2** APR A composite cell illustrates the organelles and other structures found in cells. Specialized cells differ in the numbers and types of organelles, reflecting their functions. Organelles are not drawn to scale.


Flagellum
Nucleus
Nuclear envelope
Chromatin
Nucleolus
Ribosomes
Phospholipid bilayer
Cell membrane
Microtubules
Centrioles
Mitochondrion
Rough endoplasmic reticulum
Peroxisome
Microvilli
Secretory vesicles
Golgi apparatus
Microtubule
Smooth endoplasmic reticulum
Lysosomes
Cilia
Microtubules

Molecules such as oxygen and carbon dioxide, which are soluble in lipids, can easily pass through this bilayer. However, the bilayer is impermeable to water-soluble molecules, which include amino acids, sugars, proteins, nucleic acids, and certain ions. Cholesterol molecules embedded in the cell membrane's interior help make the membrane less permeable to water-soluble substances, while their rigid structure stabilizes the membrane.

A cell membrane includes a few types of lipid molecules, but many kinds of proteins, which provide special functions. Membrane proteins are classified according to their positions. Integral proteins extend through the lipid bilayer and may protrude from one or both faces. Integral proteins that extend through both faces of the membrane are called transmembrane proteins. Peripheral membrane proteins associate outside one side of the bilayer. Membrane proteins also vary in shape—they may be globular, rodlike, or fibrous. The cell membrane is called a "fluid mosaic" because its proteins are embedded in an oily background and therefore can move, like ships on a sea. Certain types of lipids form specialized regions within the bilayer, called "rafts," to which proteins that function together may cluster, facilitating their interactions.

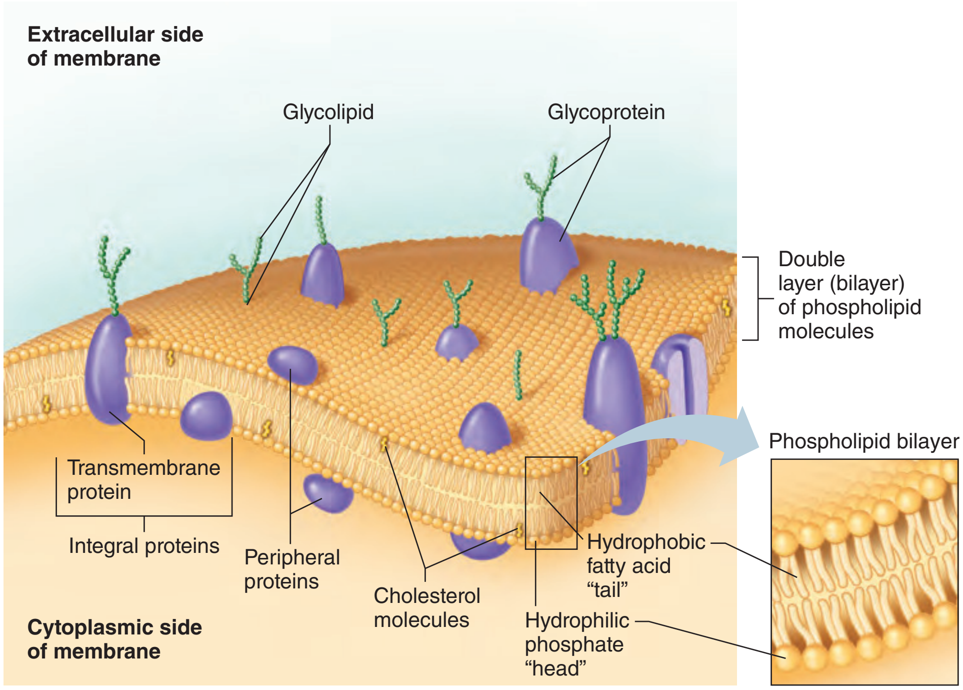

Extracellular side of membrane
Glycolipid
Glycoprotein
Double layer (bilayer) of phospholipid molecules
Phospholipid bilayer
Transmembrane protein
Integral proteins
Peripheral proteins
Cholesterol molecules
Hydrophobic fatty acid "tail"
Hydrophilic phosphate "head"
Cytoplasmic side of membrane

**FIGURE 3.3** APR The cell membrane is composed primarily of phospholipids (and some cholesterol), with proteins embedded throughout the lipid bilayer. Parts of the membrane-associated proteins that extend from the outer surface help to establish the identity of the cell as part of a particular tissue, organ, and person.

Membrane proteins have a variety of functions. Some form receptors on the cell surface that bind incoming hormones or growth factors, starting signal transduction. Receptors are structures that have specific shapes that fit and hold certain molecules. Many receptors are partially embedded in the cell membrane. Other proteins transport ions or molecules across the cell membrane. Some membrane proteins form ion channels in the phospholipid bilayer that allow only particular ions to enter or leave. Ion channels are specific for calcium ($Ca^{+2}$), sodium ($Na^{+}$), potassium ($K^{+}$), or chloride ($Cl^{-}$). A cell membrane may have a few thousand ion channels specific for each of these ions.

Many ion channels open or close like a gate under specific conditions, such as a change in electrical forces across the membrane of a nerve cell, or receiving biochemical messages from inside or outside the cell. Clinical Application 3.1 discusses how ion channels are involved in feeling—or not feeling—pain.

**FACTS OF LIFE** Ten million or more ions can pass through an ion channel in one second!

Drugs may act by affecting ion channels, and abnormal ion channels cause certain disorders. In cystic fibrosis, for example, abnormal chloride channels in cells lining the lung passageways and ducts of the pancreas cause the symptoms. Sodium channels also malfunction. The overall result: Salt trapped inside cells draws moisture into the cells and thickens surrounding mucus.

Proteins that extend inward from the inner face of the cell membrane anchor it to the protein rods and tubules that support the cell from within. Proteins that extend from the outer surface of the cell membrane mark the cell as part of a particular tissue or organ belonging to a particular person. This identification as self is important for the functioning of the immune system (see chapter 14, p. 396). Many of these proteins are attached to carbohydrates, forming glycoproteins. Another type of protein on a cell's surface is a cellular adhesion molecule (CAM), which guides a cell's interactions with other cells. For example, a series of CAMs helps a white blood cell move to the site of an injury, such as a splinter in the skin.

## Cytoplasm

The cytoplasm is the gel-like material in which organelles are suspended—it makes up most of a cell's volume. When viewed through a light microscope, cytoplasm usually appears as a clear jelly with specks scattered throughout. However, an electron microscope, which provides much greater magnification and the ability to distinguish fine detail (resolution), reveals that the cytoplasm contains networks of membranes and organelles suspended in the clear liquid *cytosol*. Cytoplasm also includes abundant protein rods and tubules that form a framework, or **cytoskeleton** (si″to-skel′e-ten), meaning "cell skeleton."

Most cell activities occur in the cytoplasm, where nutrients are received, processed, and used. The following organelles have specific functions in carrying out these activities:

### CLINICAL APPLICATION 3.1

## Too Little or Too Much Pain

The ten-year-old boy amazed the people on the streets of the small northern Pakistani town. He was completely unable to feel pain and had become a performer, stabbing knives through his arms and walking on hot coals to entertain crowds. Several other people in this community, where relatives often married relatives, were also unable to feel pain. Researchers studied the connected families and discovered a mutation that alters sodium channels in the cell membranes of certain nerve cells. The mutation blocks the channels so that the message to feel pain cannot be sent. The boy died at age thirteen from jumping off a roof. His genes could protect him from pain, but pain protects against injury by providing a warning.

A different mutation affecting the same sodium channels causes very different symptoms. In "burning man syndrome," the channels become hypersensitive, opening and flooding the body with pain easily, in response to exercise, an increase in room temperature, or just putting on socks. In another condition, "paroxysmal extreme pain disorder," the sodium channels stay open too long, causing excruciating pain in the rectum, jaw, and eyes. Researchers are using the information from these genetic studies to develop new painkillers.

1. **Endoplasmic reticulum** (en′do-plaz′mik rĕ-tik′u-lum) The endoplasmic reticulum (ER) is a complex organelle composed of membrane-bounded, flattened sacs, elongated canals, and fluid-filled, bubblelike sacs called *vesicles.* These membranous parts are interconnected and communicate with the cell membrane, the nuclear envelope, and other organelles. The ER provides a vast tubular network that transports molecules from one cell part to another. It winds from the nucleus out toward the cell membrane.

   The endoplasmic reticulum participates in the synthesis of protein and lipid molecules. These molecules may leave the cell as secretions or be used within the cell for such functions as producing new ER or cell membrane as the cell grows. The ER acts as a quality control center for the cell. Its chemical environment enables a forming protein to start to fold into the shape necessary for its function. The ER can identify and dismantle a misfolded protein, much as a defective toy might be pulled from an assembly line at a factory and discarded.

   In many places, the ER's outer membrane is studded with spherical structures called *ribosomes,* which give the ER a textured appearance when viewed with an electron microscope (fig. 3.4*a,b*). These parts of the ER are called *rough ER.* The ribosomes are sites of protein synthesis and are in the cytoplasm as well as associated with ER. Proteins being synthesized move through ER tubules to another organelle, the Golgi apparatus, for further processing.

   As the ER nears the cell membrane, it becomes more cylindrical and ribosomes become sparse and then are no longer associated with the ER. This section of the ER is called *smooth ER* (fig. 3.4*c*). Along the smooth ER are enzymes that are important in lipid synthesis, absorption of fats from the digestive tract, and the metabolism of drugs. Cells that break down drugs and alcohol, such as liver cells, have extensive networks of smooth ER.
2. **Ribosomes** (ri′bo-sōmz) Ribosomes, where protein synthesis occurs, are attached to ER membranes or are scattered throughout the cytoplasm (see fig. 3.2). Clusters of ribosomes in the cytoplasm, called *polysomes,* enable a cell to quickly manufacture proteins required in large amounts. All ribosomes are composed of protein and RNA molecules. Ribosomes provide enzymatic activity as well as a structural support for the RNA molecules that come together as the cell links amino acids to form proteins, discussed in chapter 4 (pp. 95–99).
3. **Golgi apparatus** (gol′je ap″ah-ra′tus) The Golgi apparatus is a stack of about six flattened, membranous sacs (figs. 3.2 and 3.5). This organelle refines, packages, and transports proteins synthesized on ribosomes associated with the ER. Proteins arrive at the Golgi apparatus enclosed in vesicles (sacs) composed of the ER membrane. These vesicles fuse with the membrane at the innermost end of the Golgi apparatus, which is specialized to receive glycoproteins.

   Sugars are added to many proteins that pass through the stacks of Golgi membrane, forming glycoproteins that may stabilize the protein or enable it to fold into a form that makes it functional. When the glycoproteins reach the outermost layer, they are packaged in bits of Golgi membrane, which bud off and form bubblelike transport vesicles. Such a vesicle may then move to and fuse with the cell membrane, releasing its contents to the outside as a secretion (figs. 3.2 and 3.5). This process is called *exocytosis* (see page 76).

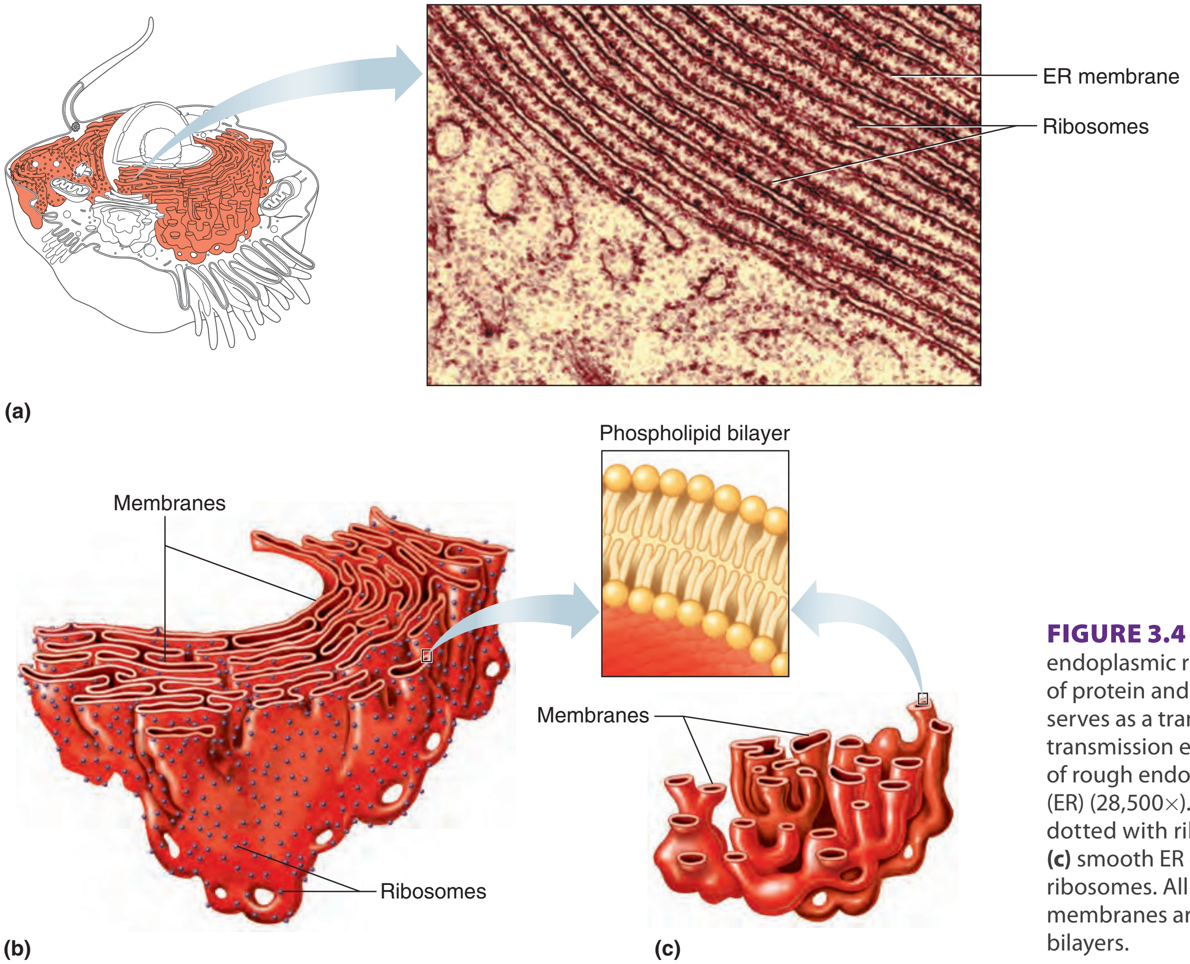


**FIGURE 3.4** APR The endoplasmic reticulum is the site of protein and lipid synthesis, and serves as a transport system. **(a)** A transmission electron micrograph of rough endoplasmic reticulum (ER) (28,500×). **(b)** Rough ER is dotted with ribosomes, whereas **(c)** smooth ER does not have ribosomes. All intracellular membranes are phospholipid bilayers.

Researchers are creating "artificial organelles" to use in industrial processes and to better understand how cells work. Artificial ribosomes, ER, and Golgi apparatuses, which are part of the secretory network, can produce protein if given genetic information. The first protein manufactured on artificial ribosomes was firefly luciferase, responsible for the insect's famous "glow."

## PRACTICE

4. What is a *selectively permeable membrane?*
5. Describe the chemical structure of a cell membrane.
6. What are the functions of the endoplasmic reticulum?
7. What are the functions of the Golgi apparatus?
8. Explain how organelles and other structures interact to secrete substances from the cell.

4. **Mitochondria** (mi″to-kon′dre-ah; *sing.* mi″to-kon′dre-on) Mitochondria are elongated, fluid-filled sacs that vary in size and shape. They can move slowly through the cytoplasm and reproduce by dividing. A mitochondrion has an outer and an inner layer (figs. 3.2 and 3.6). The inner layer is folded extensively into partitions called *cristae*. Connected to the cristae are enzymes that control some of the chemical reactions that release energy from certain nutrient molecules in a process called cellular respiration. Mitochondria are the major sites of chemical reactions that capture and store this energy in the chemical bonds of adenosine triphosphate (ATP). A cell can easily use energy stored as ATP. This is why very active cells, such as muscle cells, have thousands of mitochondria. (Chapter 4, p. 91, describes this energy-releasing function in more detail.) Mitochondria contain a small amount of their own DNA.

A person inherits mitochondria only from the mother because these organelles are excluded from the part of a sperm cell that enters an egg cell.

5. **Lysosomes** (li′so-sōmz) Lysosomes are tiny, enzyme-containing membranous sacs that bud off of sections of Golgi membranes (see fig. 3.2). They have an acidic pH that enables the lysosomal enzymes to function. The powerful lysosomal

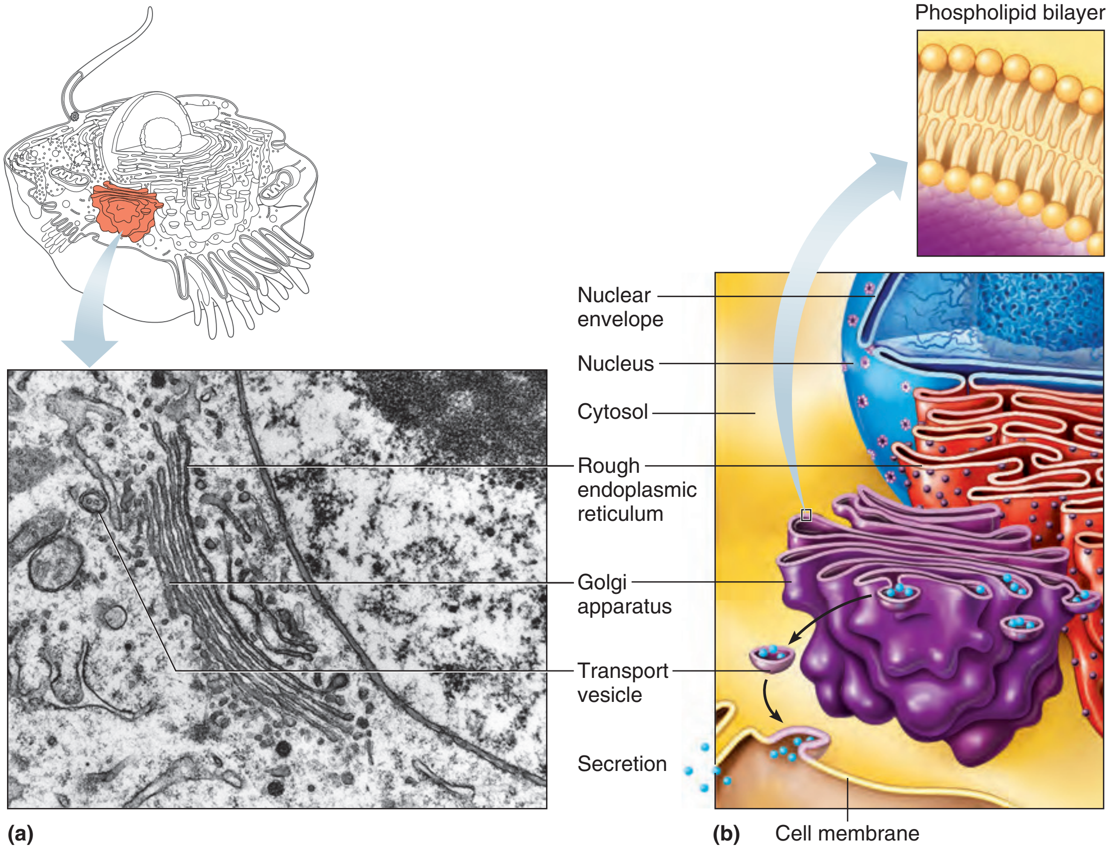

Phospholipid bilayer
Nuclear envelope
Nucleus
Cytosol
Rough endoplasmic reticulum
Golgi apparatus
Transport vesicle
Secretion
(a)
(b)
Cell membrane

**FIGURE 3.5** APR The Golgi apparatus processes secretions. **(a)** A transmission electron micrograph of a Golgi apparatus (48,500×). **(b)** The Golgi apparatus consists of membranous sacs that continually receive vesicles from the endoplasmic reticulum and produce vesicles that enclose secretions. All intracellular membranes are phospholipid bilayers.

enzymes break down nutrient molecules or foreign particles. Certain white blood cells, for example, engulf bacteria, which lysosomal enzymes digest. In liver cells, lysosomes break down cholesterol, toxins, and drugs. Lysosomes also destroy worn cellular parts in a process called "autophagy," which means "eating self." Genetics Connection 3.1 describes disorders that result from deficiencies of lysosomal enzymes. APR

6. **Peroxisomes** (pĕ-roks′ĭ-sōmz) These membranous sacs are abundant in liver and kidney cells. They house enzymes (different from those in lysosomes) that catalyze (speed) a variety of biochemical reactions, including breakdown of hydrogen peroxide (a by-product of metabolism) and fatty acids, and detoxification of alcohol.

Vesicles that deliver proteins and lipids to other cells are called *exosomes*. These vesicles remove debris, transport immune system molecules from cell to cell, and provide a vast communication network among cells.

7. **Microfilaments and microtubules** Microfilaments and microtubules are two types of thin, threadlike strands in the cytoplasm. They form the cytoskeleton and are also part of certain structures that have specialized activities.

   Microfilaments are tiny rods of a protein called actin. They form meshworks or bundles, and provide cell motility (movement). In muscle cells, for example, microfilaments aggregate to form

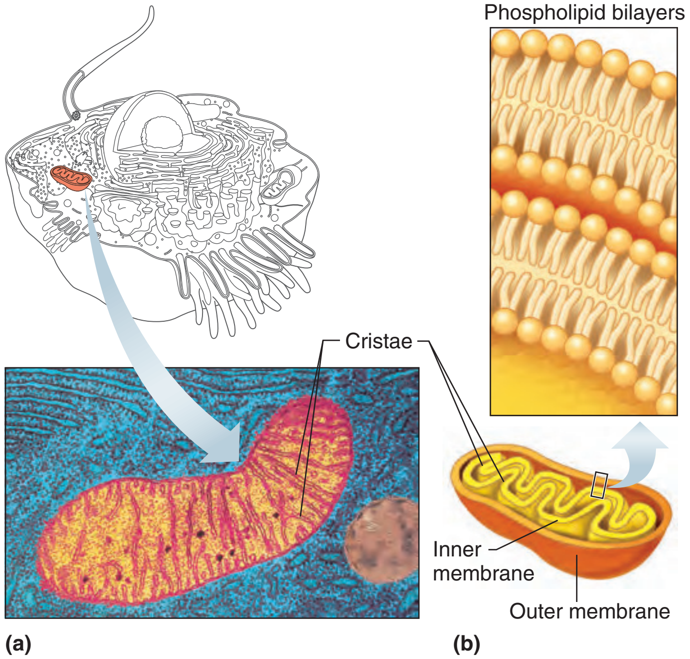

Phospholipid bilayers
Cristae
Inner membrane
Outer membrane
(a)
(b)

**FIGURE 3.6** APR A mitochondrion is a major site of energy reactions. **(a)** A transmission electron micrograph of a mitochondrion (28,000×). **(b)** Cristae partition this saclike organelle. All intracellular membranes are phospholipid bilayers.

GENETICS CONNECTION 3.1

## Lysosomal Storage Diseases

The little boy was born in 1997, and at first he cried frequently and had difficulty feeding, and his limbs were stiff. His mental and motor skill development slowed and then stopped. At nine months old, he was diagnosed with Krabbe disease, which he had inherited from his parents, who are carriers. His lysosomes could not make an enzyme that is necessary to produce myelin, a lipid that insulates neurons. As a result, his neurons did not have enough myelin. Krabbe disease is a type of inherited illness called a leukodystrophy, which means that it affects the white matter of the brain.

By the time of diagnosis, damage to the boy's nervous system was already advanced. He ceased moving and responding, lost hearing and vision, and had to be tube fed. The boy lived for eight years. Had he been born today, he would have been tested for Krabbe disease along with dozens of other such "inborn errors of metabolism" with a few drops of blood taken from his heel shortly after birth. A stem cell transplant from a donor's umbilical cord blood may have prevented his symptoms.

Lysosomes house 43 different types of enzymes, and so 43 different types of disorders are "lysosomal storage diseases," a subtype of inborn errors of metabolism. Each enzyme must be present within a certain concentration range in order for the cell to function properly. Although each of the disorders is rare, together they affect about 10,000 people worldwide. Some lysosomal storage diseases can be treated by replacing the enzyme, using a drug to reduce the biochemical buildup, or using a drug that can unfold and correctly refold a misfolded enzyme, enabling it to function.

*myofibrils,* which help these cells contract (see chapter 8, p. 190).

Microtubules are long, slender tubes with diameters two or three times those of microfilaments (fig. 3.7). Microtubules are composed of molecules of a globular protein called *tubulin*, attached in a spiral to form a long tube. They are important in cell division. Intermediate filaments lie between microfilaments and microtubules in diameter, and are made of different proteins in different cell types. They are abundant in skin cells and neurons, but scarce in other cell types.

8. **Centrosome** (sen′tro-sōm) The centrosome is a structure near the Golgi apparatus and nucleus. It is nonmembranous and consists of two hollow cylinders, called *centrioles,* which are composed of microtubules organized in nine groups of three (figs. 3.2 and 3.8). The centrioles lie at right angles to each other. During mitosis, the centrioles distribute chromosomes to newly forming cells.
9. **Cilia and flagella** Cilia and flagella are motile structures that extend from the surfaces of certain cells. They are composed of microtubules in a "9 + 2" array, similar to centrioles but with two additional microtubules in the center. Cilia and flagella are similar structures that differ mainly in length and abundance.

   Cilia fringe the free surfaces of some cells. A cilium is hairlike and anchored beneath the cell membrane (see fig. 3.2). Cilia form in precise patterns. They move in a coordinated "to-and-fro" manner, so that rows of them beat in succession, producing a wave of motion. This wave moves fluids, such as mucus, over the surface of certain tissues (fig. 3.9*a*). Early in development, beating cilia control the movements of cells as they join to form organs. Some cilia have receptors that detect molecules that signal sensations to cells.

   Flagella are much longer than cilia, and usually a cell has only one (see fig. 3.2). A flagellum moves in an undulating wave, which begins at its base. The tail of a sperm cell is a flagellum that enables the cell to "swim." The sperm tail is the only flagellum in humans (fig. 3.9*b*).

The cilia that wave secretions out of the respiratory system or move an egg toward the uterus are called motile cilia. Another subtype of this organelle, called a primary or nonmotile cilium, functions as a "cellular antenna," sensing signals and sending them into cells to control growth and maintain tissues. Compared to the many motile cilia that fringe cells, primary cilia may be one per cell. Evidence that primary cilia are important is that the cells of nearly all species have them, nearly all human cell types have them, and diseases in which they are abnormal typically affect several organ systems. Such conditions are called ciliopathies—"sick cilia."

10. **Vesicles** (ves′ĭ-klz) Vesicles are membranous sacs that store or transport substances within a cell and between cells. Larger vesicles that contain mostly water form from part of the cell membrane folding inward and pinching off, carrying liquid or solid material from outside the cell into the

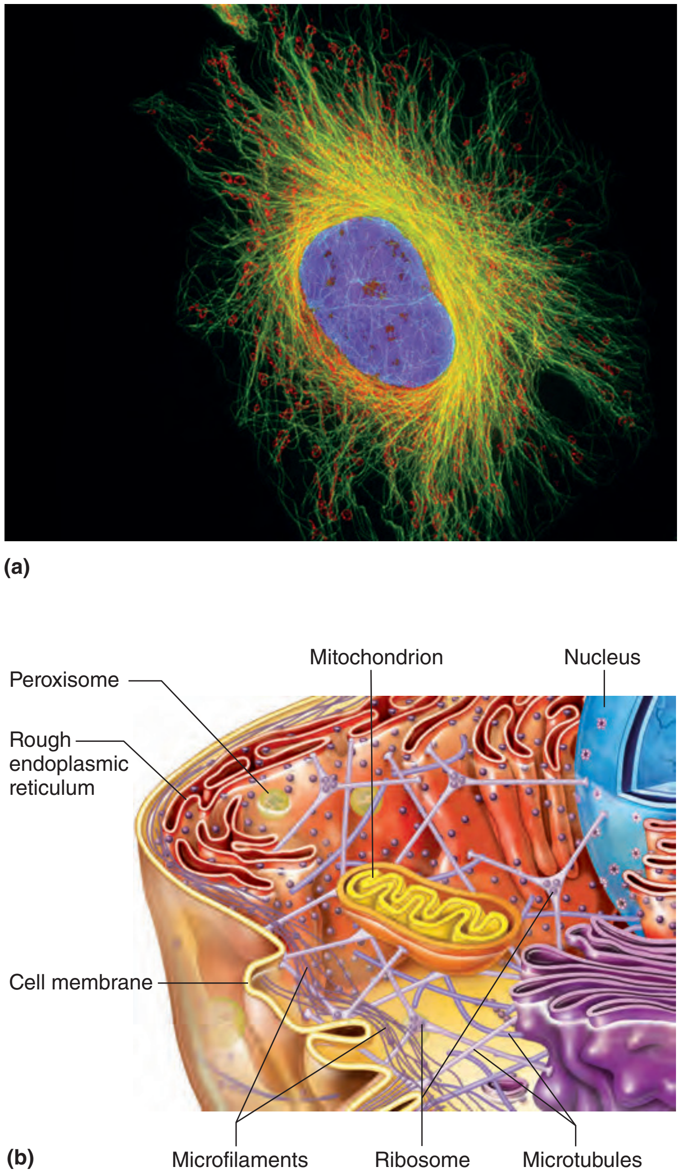


**FIGURE 3.7** APR The cytoskeleton provides an inner framework for a cell. **(a)** In this falsely colored micrograph the cytoskeleton is yellow and red (3,000×). The membrane is not visible. **(b)** Microtubules built of tubulin and microfilaments built of actin help maintain the shape of a cell by forming a scaffolding beneath the cell membrane and in the cytoplasm.

cytoplasm. Smaller vesicles shuttle material from the rough ER to the Golgi apparatus as part of secretion (see fig. 3.2).

## PRACTICE

9. Describe a mitochondrion.
10. What is the function of a lysosome?
11. How do microfilaments and microtubules differ?
12. What is a centrosome and what does it do?
13. Locate cilia and flagella and explain what they are composed of and what they do.
14. Describe functions of vesicles.

## Cell Nucleus

The nucleus houses the genetic material (DNA), which directs all cell activities (figs. 3.2 and 3.10). It is a large, roughly spherical structure enclosed in a double-layered **nuclear envelope,** which consists of inner and outer lipid bilayer membranes. The nuclear envelope has protein-lined channels called *nuclear pores* that allow certain molecules to exit the nucleus. A nuclear pore is not just a hole, but a complex opening formed from 100 or so types of proteins. A nuclear pore is large enough to let out the RNA molecules that carry genes' messages, but not large enough to let out the DNA itself, which must remain in the nucleus to maintain the genetic instruction set.

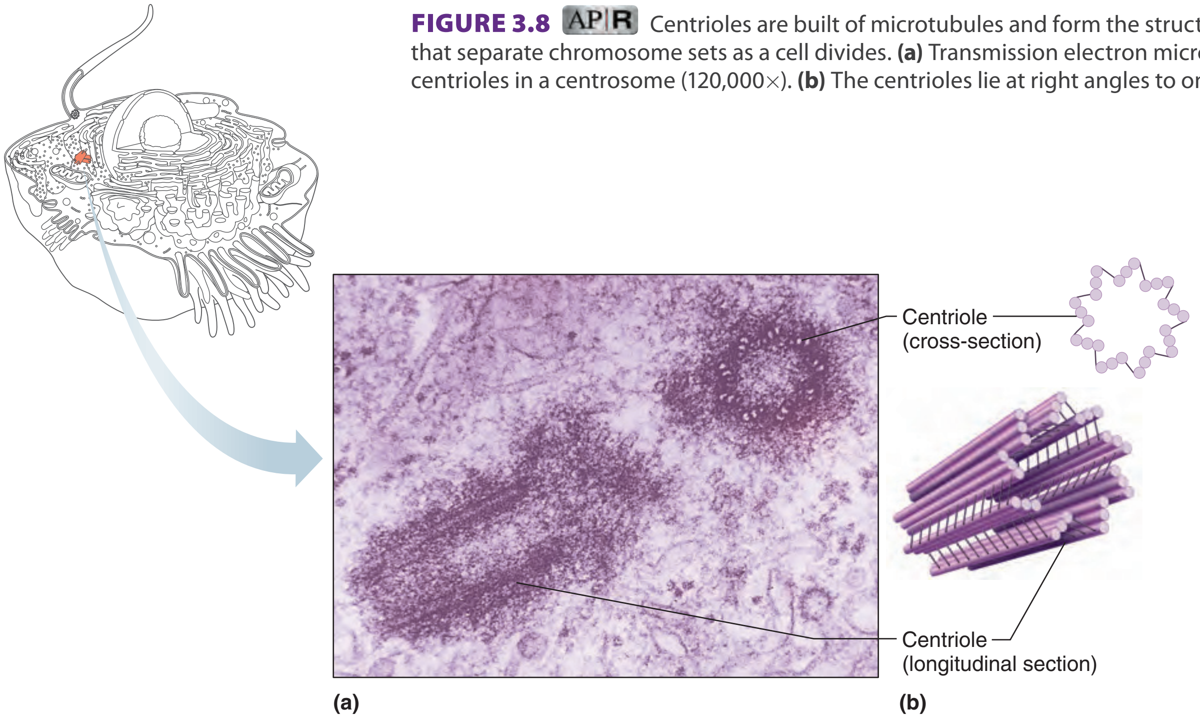


**FIGURE 3.8** APR Centrioles are built of microtubules and form the structures (spindle fibers) that separate chromosome sets as a cell divides. **(a)** Transmission electron micrograph of the two centrioles in a centrosome (120,000×). **(b)** The centrioles lie at right angles to one another.

The nucleus contains a fluid, called *nucleoplasm,* in which the following structures are suspended:

1. **Nucleolus** (nu-kle′o-lus) A nucleolus ("little nucleus") is a small, dense body composed largely of RNA and protein. It has no surrounding membrane and forms in specialized regions of certain chromosomes. Ribosomes form in the nucleolus and then migrate through nuclear pores to the cytoplasm.
2. **Chromatin** Chromatin consists of loosely coiled fibers of DNA and protein that condense to form structures called **chromosomes** (kro′mo-sōmz).

The DNA contains the information for protein synthesis. When the cell begins to divide, chromatin fibers coil tightly, and individual chromosomes become visible when stained and viewed under a light microscope. At other times, chromatin unwinds locally to permit the information in certain genes (DNA sequences) to be accessed. Table 3.1 summarizes the structures and functions of cell parts.

### PRACTICE

15. Identify the structure that separates the nuclear contents from the cytoplasm.
16. What is produced in the nucleolus?
17. Describe chromatin and how it changes.

## 3.3 Movements Through Cell Membranes

The cell membrane is a selective barrier that controls which substances enter and leave the cell. Movements of substances into and out of cells include passive mechanisms that do not require cellular energy (diffusion, facilitated diffusion, osmosis, and filtration) and active mechanisms that use cellular energy (active transport, endocytosis, and exocytosis). Transport of substances across the cell membrane is particularly important in the functioning of the nervous, muscular, endocrine, and digestive systems.

### Passive Mechanisms

#### *Diffusion*

**Diffusion** (dĭ-fu′zhun) (also called *simple diffusion*) is the tendency of molecules or ions in a liquid solution or air to move from regions of higher concentration to regions of lower concentration. As the particles move farther apart, they become more evenly distributed, or more *diffuse.* Diffusion occurs because molecules and ions are in constant motion. Each particle travels in a separate path along a straight line until it collides and bounces off another particle, changing direction, then colliding and changing direction once more. At body temperature, small molecules such as water move more than a thousand miles per hour. A single molecule may collide with other molecules a million times each second.

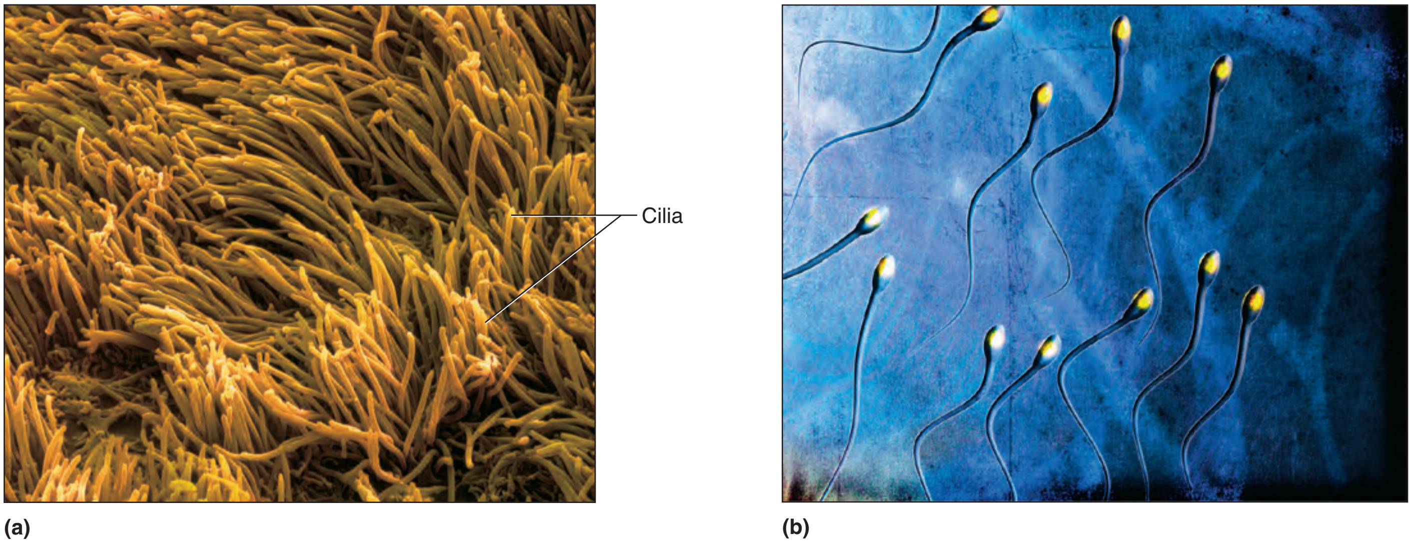


**FIGURE 3.9** Cilia and flagella provide movement. **(a)** Cilia are motile, hairlike extensions that fringe the surfaces of certain cells, including those that form the inner lining of the respiratory tubes (5,800×). Cilia remove debris from the respiratory tract with their sweeping, to-and-fro movement. **(b)** Flagella form the tails of these human sperm cells, enabling them to "swim" (840×).

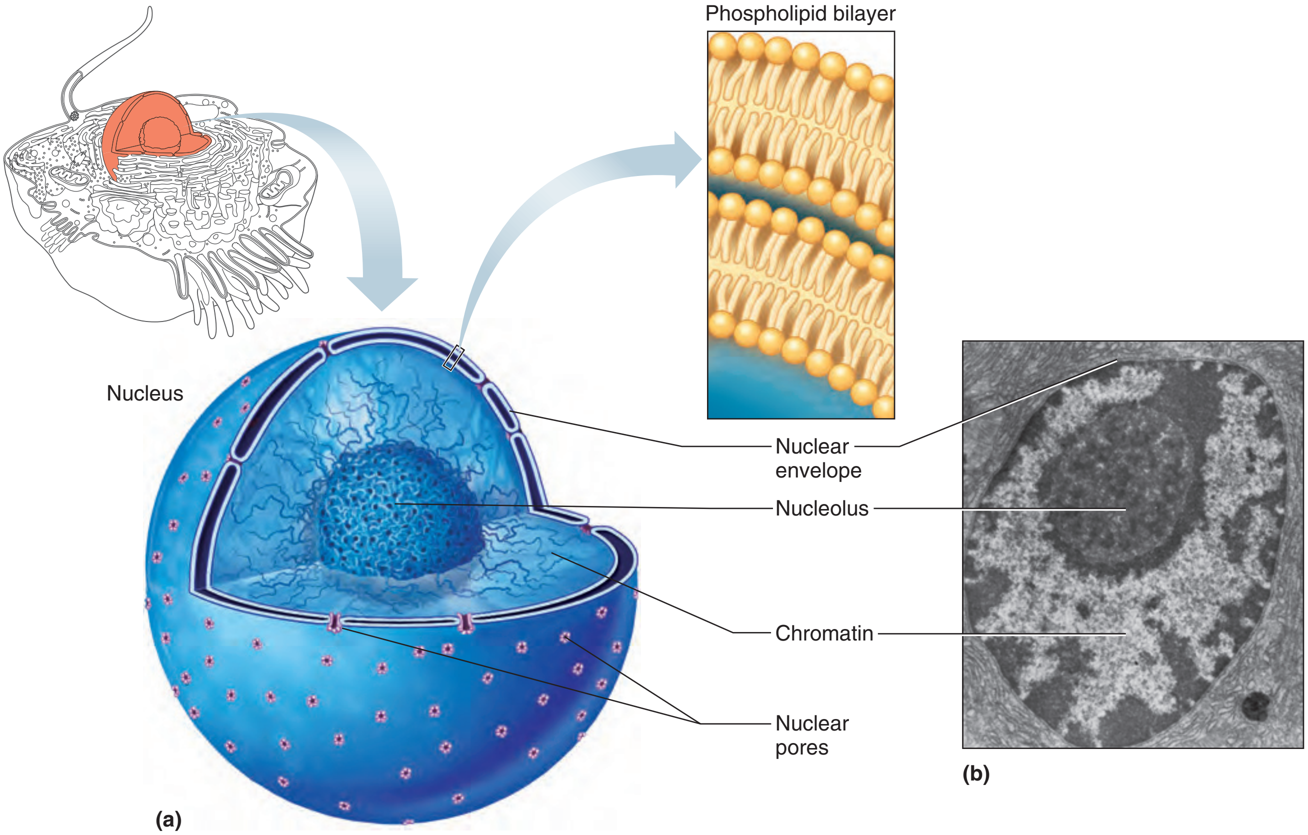

Phospholipid bilayer
Nucleus
Nuclear envelope
Nucleolus
Chromatin
Nuclear pores
(a)
(b)

**FIGURE 3.10** APR The nucleus. **(a)** The nuclear envelope is selectively permeable and allows certain substances to pass between the nucleus and the cytoplasm. Nuclear pores are more complex than depicted here. All intracellular membranes are phospholipid bilayers. **(b)** Transmission electron micrograph of a cell nucleus (7,500×). It contains a nucleolus and masses of chromatin.

Q *What structures are inside the nucleus of a cell?*

**Answer can be found in Appendix F on page 582.**

Collisions are less likely if a solution has fewer particles, so there is a net movement of particles from a region of higher concentration to a region of lower concentration. The difference in concentration is called a *concentration gradient,* and diffusion occurs down a concentration gradient. With time, the concentration of a given substance becomes uniform throughout a solution. This state is called *diffusional equilibrium* (dĭ-fu′zhunl e″kwĭ-lib′re-um). Random movements continue, but there is no further net movement, and the concentration of a substance is uniform throughout the solution.

Sugar (a solute) in a sugar cube put in a glass of water (a solvent) illustrates diffusion (fig. 3.11). At first the sugar remains highly concentrated at the bottom of the

### TABLE 3.1 Structures and Functions of Cell Parts

| Cell Part(s) | Structure | Function |
|---|---|---|
| Cell membrane | Membrane composed of protein and lipid molecules | Maintains integrity of cell and controls passage of materials into and out of cell |
| Endoplasmic reticulum | Complex of interconnected membrane-bounded sacs and canals | Transports materials within the cell, provides attachment for ribosomes, and synthesizes lipids |
| Ribosomes | Particles composed of protein and RNA molecules | Synthesize proteins |
| Golgi apparatus | Group of flattened, membranous sacs | Packages protein molecules for transport and secretion |
| Mitochondria | Membranous sacs with inner partitions | Release energy from nutrient molecules and change energy into a usable form |
| Lysosomes | Membranous sacs | Digest worn cellular parts or substances that enter cells |
| Peroxisomes | Membranous sacs | House enzymes that catalyze diverse reactions, including breakdown of hydrogen peroxide and fatty acids, and alcohol detoxification |
| Microfilaments and microtubules | Thin rods and tubules | Support the cytoplasm and help move substances and organelles within the cytoplasm |
| Centrosome | Nonmembranous structure composed of two rodlike centrioles | Helps distribute chromosomes to new cells during cell division |
| Cilia and flagella | Motile projections attached beneath the cell membrane | Cilia propel fluid over cellular surfaces, and a flagellum enables a sperm cell to move |
| Vesicles | Membranous sacs | Contain and transport various substances |
| Nuclear envelope | Double membrane that separates the nuclear contents from the cytoplasm | Maintains integrity of nucleus and controls passage of materials between nucleus and cytoplasm |
| Nucleolus | Dense, nonmembranous body composed of protein and RNA | Site of ribosome synthesis |
| Chromatin | Fibers composed of protein and DNA | Contains information for synthesizing proteins |

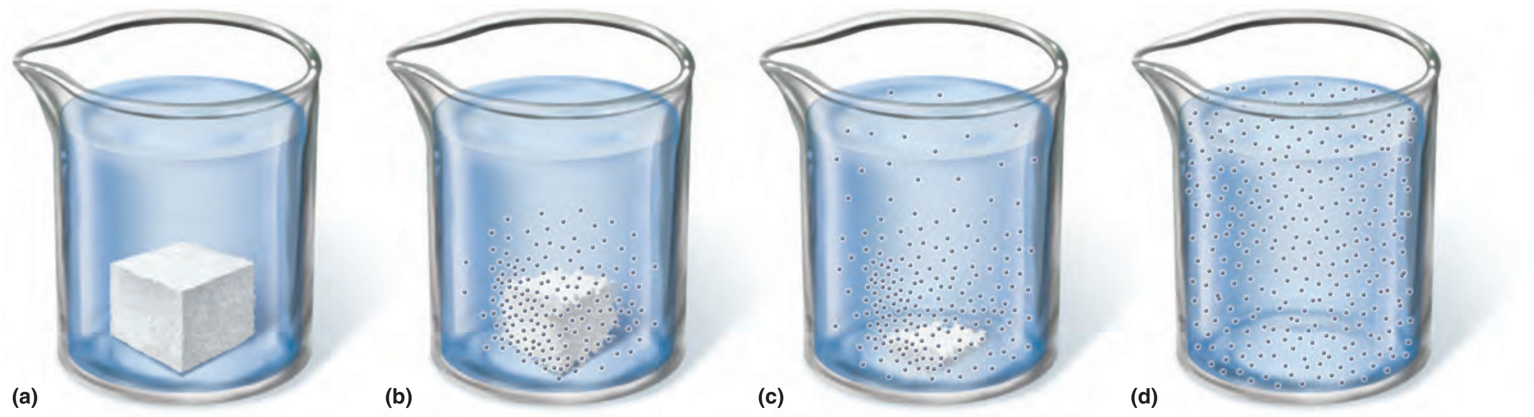


**FIGURE 3.11** A dissolving sugar cube illustrates diffusion. **(a–c)** A sugar cube placed in water slowly disappears as the sugar molecules dissolve and then diffuse from regions where they are more concentrated toward regions where they are less concentrated. **(d)** Eventually the sugar molecules are distributed evenly throughout the water.

glass. Diffusion moves the sugar molecules from the area of high concentration and disperses them into solution among the moving water molecules. Eventually, the sugar molecules become uniformly distributed in the water.

Diffusion of a substance across a membrane can happen only if (1) the membrane is permeable to that substance, and (2) a concentration gradient exists such that the substance is at a higher concentration on one side of the membrane or the other (fig. 3.12). Consider oxygen and carbon dioxide, to which cell membranes are permeable. In the body, oxygen diffuses into cells and carbon dioxide diffuses out of cells, but equilibrium is never reached. Intracellular oxygen is always low because oxygen is constantly used up in metabolic reactions. Extracellular oxygen is maintained at a high level by homeostatic mechanisms in the respiratory and cardiovascular systems. Thus, a concentration gradient always allows oxygen to diffuse into cells.

The level of carbon dioxide, which is a metabolic waste product, is always high inside cells. Homeostasis maintains a lower extracellular carbon dioxide level, so a concentration gradient always favors carbon dioxide diffusing out of cells (fig. 3.13).

---

*Dialysis* is a technique that uses diffusion to separate small molecules from larger ones in a liquid. The artificial kidney uses a variant of this process—*hemodialysis*—to treat patients suffering from kidney damage or failure. An artificial kidney (dialyzer) passes blood from a patient through a long, coiled tubing composed of porous cellophane. The size of the pores allows smaller molecules carried in the blood, such as the waste material urea, to exit through the tubing, while larger molecules, such as those of blood proteins, remain inside the tubing. The tubing is submerged in a tank of dialyzing fluid (wash solution), which contains varying concentrations of different chemicals. Altering the concentrations of molecules in the dialyzing fluid can control which molecules diffuse out of blood and which remain in it.

---

### Facilitated Diffusion

Substances that are not able to pass through the lipid bilayer need the help of membrane proteins to get across, a process known as **facilitated diffusion** (fah-sil″ĭ-tāt′ed dĭ-fu′zhun) (fig. 3.14). One form of facilitated diffusion uses the ion channels described earlier. Molecules such as glucose and amino acids are not lipid-soluble, but are too large to pass through membrane channels. They enter cells by another form of facilitated diffusion that uses a carrier molecule. For example, a glucose molecule outside a cell combines with a special protein carrier molecule at the surface of the cell membrane. The union of the glucose and the carrier molecule changes the shape of the carrier, enabling it to move glucose to the other side of the membrane. The carrier releases the glucose and then returns to its original shape and picks up another glucose molecule. The hormone *insulin,* discussed in chapter 11 (p. 318), promotes facilitated diffusion of glucose through the membranes of certain cells.

Facilitated diffusion is similar to simple diffusion in that it only moves molecules from regions of higher concentration toward regions of lower concentration. The number of carrier molecules in the cell membrane limits the rate of facilitated diffusion, which occurs in most cells.

### Osmosis

**Osmosis** (oz-mo′sis) is the movement of water across a selectively permeable membrane into a compartment containing solute that cannot cross the same membrane. The mechanism of osmosis is complex, but in part involves the diffusion of water down its concentration gradient. In the following example, assume that the selectively permeable membrane is permeable to water molecules (the solvent) but impermeable to protein molecules (the solute).

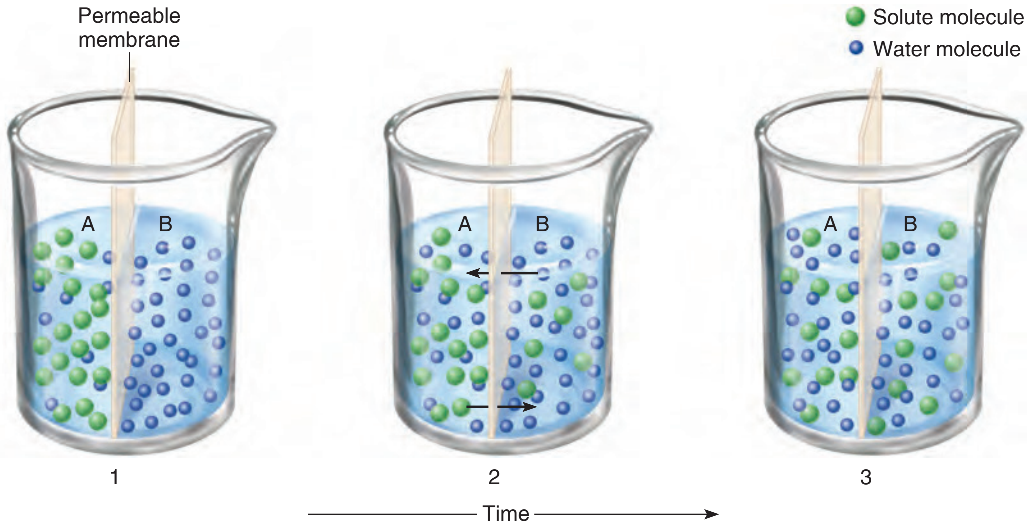


**FIGURE 3.12** AP|R Diffusion is a passive movement of molecules. **(1)** A membrane permeable to water and solute molecules separates a container into two compartments. Compartment *A* contains both types of molecules, while compartment *B* contains only water molecules. **(2)** As a result of molecular motions, solute molecules tend to diffuse from compartment *A* into compartment *B*. Water molecules tend to diffuse from compartment *B* into compartment *A*. **(3)** Eventually equilibrium is reached.

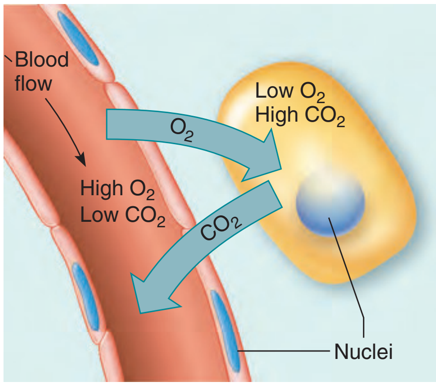


**FIGURE 3.13** Diffusion enables oxygen to enter cells and carbon dioxide to leave.

In solutions, a higher concentration of solute (protein in this case) means a lower concentration of water; a lower concentration of solute means a higher concentration of water. This is because solute molecules take up space that water molecules would otherwise occupy.

Like molecules of other substances, molecules of water diffuse from areas of higher concentration to areas of lower concentration. In figure 3.15, the greater concentration of protein in compartment *A* means that the water concentration there is less than the concentration of pure water in compartment *B*. Therefore, water diffuses from compartment *B* across the selectively permeable membrane and into compartment *A*. In other words, water moves from compartment *B* into compartment *A* by osmosis. Protein, on the other hand, cannot move out of compartment *A* because the selectively permeable membrane is impermeable to it. Note in figure 3.15 that as osmosis occurs, the water level on side *A* rises. This ability of osmosis to generate enough pressure to lift a volume of water is called *osmotic pressure.*

The greater the concentration of impermeant solute particles (protein in this case) in a solution, the greater the osmotic pressure. Water always tends to move toward solutions of greater osmotic pressure. That is, water moves by osmosis toward regions of trapped solute—whether in a laboratory exercise or in the body.

Cell membranes are generally permeable to water, so water equilibrates by osmosis throughout the body, and the concentration of water and solutes everywhere in the intracellular and extracellular fluids is essentially the same. Therefore, the osmotic pressure of the intracellular and extracellular fluids is the same. Any solution that has the same osmotic pressure as body fluids is called **isotonic** (fig. 3.16*a*).

Solutions that have a higher osmotic pressure than body fluids are called **hypertonic.** If cells are put into a hypertonic solution, water moves by osmosis out of the cells into the surrounding solution, and the cells shrink (fig. 3.16*b*). Conversely, cells put into a **hypotonic** solution, which has a lower osmotic pressure than body fluids, gain water by osmosis, and they swell (fig. 3.16*c*).

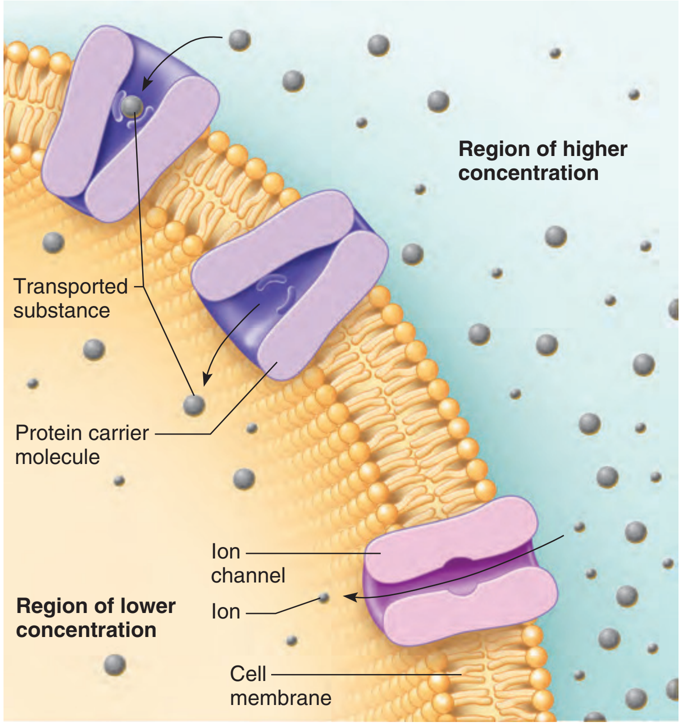


**FIGURE 3.14** APR Facilitated diffusion uses carrier molecules to transport some substances into or out of cells, from a region of higher concentration to one of lower concentration.

If the concentration of solute in solutions that are infused into body tissues or blood is not controlled, osmosis may swell or shrink cells, impairing their function. For instance, if red blood cells are placed in distilled water (which is hypotonic to them), the cells gain water by osmosis, and they may burst (hemolyze). Yet red blood cells exposed to 0.9% NaCl solution (normal saline) do not change shape because this solution is isotonic to human cells. A red blood cell in a hypertonic solution shrinks.

### *Filtration*

Molecules move through membranes by diffusion because of random movements. In other instances, the process of **filtration** (fil-tra′shun) forces molecules through membranes.

Filtration is commonly used to separate solids from water. One method is to pour a mixture of solids and water onto filter paper in a funnel. The paper is a porous membrane through which the small water molecules can pass, leaving the larger solid particles behind. *Hydrostatic pressure,* created by the weight of water due to gravity, forces the water molecules through to the other side. A familiar example of filtration is making coffee by the drip method.

In the body, tissue fluid forms when water and small dissolved substances are forced out through the thin, porous walls of blood capillaries, but larger particles, such as blood protein molecules, are left inside

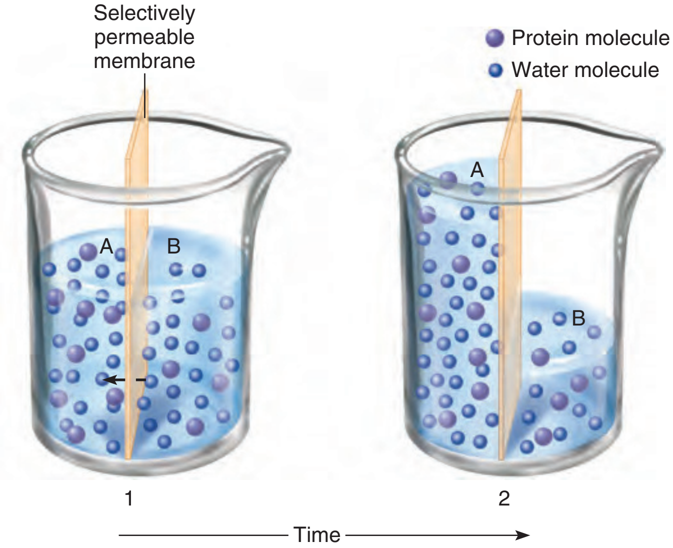


**FIGURE 3.15** APR Osmosis. **(1)** A selectively permeable membrane separates the container into two compartments. At first, compartment *A* contains a higher concentration of protein (and a lower concentration of water) than compartment *B*. Water moves by osmosis from compartment *B* into compartment *A*.
**(2)** The membrane is impermeable to proteins, so equilibrium can be reached only by movement of water. As water accumulates in compartment *A*, the water level on that side of the membrane rises.

(fig. 3.17). The force for this movement comes from blood pressure, generated largely by heart action, which is greater inside the vessel than outside it. However, the impermeant proteins tend to hold water in blood vessels by osmosis, thus preventing formation of excess tissue fluid, a condition called **edema.** Filtration also helps the kidneys cleanse blood.

## PRACTICE

18. What types of substances diffuse most readily through a cell membrane?
19. Explain the differences among diffusion, facilitated diffusion, and osmosis.
20. Distinguish among hypertonic, hypotonic, and isotonic solutions.
21. How does filtration happen in the body?

## Active Mechanisms

When molecules or ions pass through cell membranes by diffusion or facilitated diffusion, their net movements are from regions of higher concentration to regions of lower concentration. Sometimes, however, particles move from a region of lower concentration to one of higher concentration. This requires energy, which comes from cellular metabolism and, specifically, from a molecule called adenosine triphosphate (ATP). The situation is a little like requiring a push to enter a crowded room.

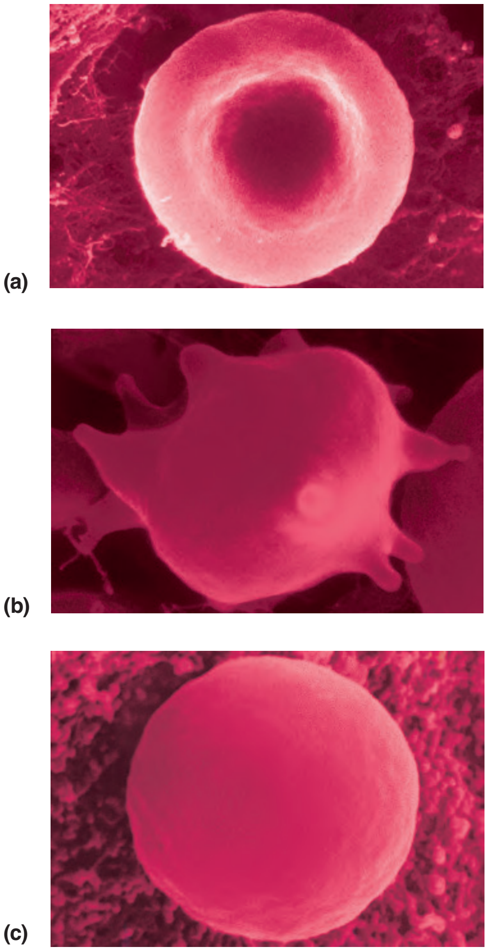


**FIGURE 3.16** APR When red blood cells are placed **(a)** in an isotonic solution, the cells maintain their characteristic shapes. **(b)** In a hypertonic solution, cells shrink. **(c)** In a hypotonic solution, cells swell and may burst (5,000×).

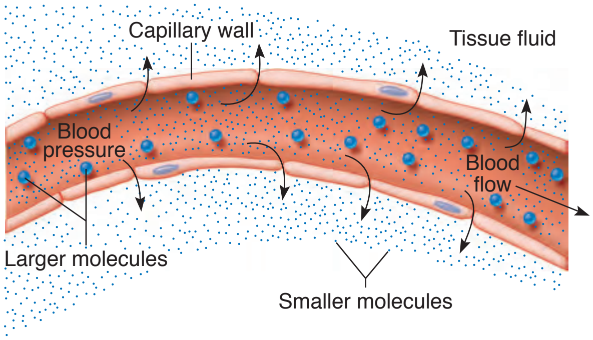


**FIGURE 3.17** Blood pressure forces smaller molecules through tiny openings in the capillary wall. The larger molecules remain inside.

### *Active Transport*

**Active transport** (ak′tiv trans′port) is a process that moves particles through membranes from a region of lower concentration to a region of higher concentration. Sodium ions, for example, can diffuse slowly through cell membranes, but their concentration typically remains much greater outside cells than inside cells. This is because active transport continually moves sodium ions through cell membranes from regions of lower concentration (inside) to regions of higher concentration (outside).

Active transport is similar to facilitated diffusion in that it uses specific carrier molecules in cell membranes (fig. 3.18). It differs from facilitated diffusion in that particles move from regions of low concentration to regions of high concentration, and energy from ATP is required. Up to 40% of a cell's energy supply may be used to actively transport particles through its membranes.

The carrier molecules in active transport are proteins with binding sites that combine with the particles being transported. Such a union triggers the release of energy, and this alters the shape of the carrier protein. As a result, the "passenger" particles move through the membrane. Once on the other side, the transported particles are released, and the carriers can accept other passenger molecules at their binding sites. Because these carrier proteins transport substances from regions of low concentration to regions of high concentration, they are sometimes called "pumps."

Particles that are actively transported across cell membranes include sugars and amino acids as well as sodium, potassium, calcium, and hydrogen ions. Some of these substances are actively transported into cells, and others are actively transported out.

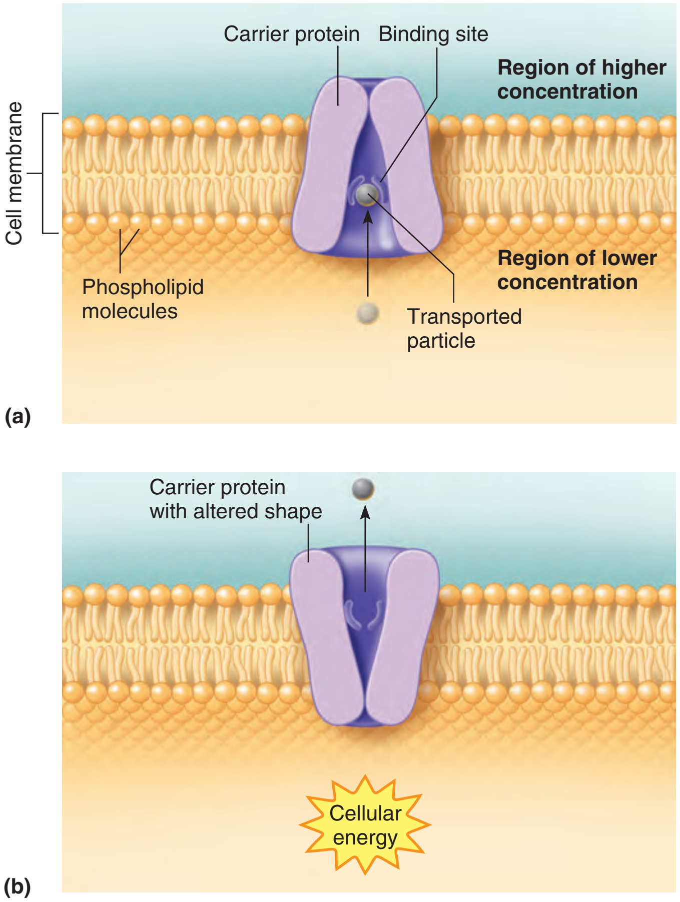


**FIGURE 3.18** APR Active transport moves molecules against their concentration gradient. **(a)** During active transport, a molecule or an ion combines with a carrier protein, whose shape changes as a result. **(b)** This process, which requires cellular energy, transports the particle across the cell membrane.

Q *What are two requirements for active transport to occur?*
**Answer can be found in Appendix F on page 582.**

### *Endocytosis and Exocytosis*

Two processes use cellular energy to move substances into or out of a cell without actually crossing the cell membrane. In **endocytosis** (en″do-si-to′sis), molecules or other particles that are too large to enter a cell by diffusion or active transport are conveyed in a vesicle that forms from a portion of the cell membrane. In **exocytosis** (ek″so-si-to′sis), the reverse process secretes a substance stored in a vesicle from the cell. Nerve cells use exocytosis to release the neurotransmitter chemicals that signal other nerve cells, muscle cells, or glands.

Endocytosis and exocytosis can act together, bringing a particle into a cell, and escorting it, in a vesicle, out of the cell at another place in the cell membrane. This process is called transcytosis. HIV can enter the body this way.

Endocytosis happens in three ways: pinocytosis, phagocytosis, and receptor-mediated endocytosis. In **pinocytosis** (pi″no-si-to′sis), meaning "cell drinking," cells take in droplets of liquid from their surroundings, as a small portion of the cell membrane indents. The open end of the tubelike part that forms seals off and produces a small vesicle, which detaches from the membrane surface and moves into the cytoplasm. Eventually the vesicular membrane breaks down, and the liquid inside becomes part of the cytoplasm. In this way, a cell can take in water and the molecules dissolved in it, such as proteins, that otherwise might be too large to enter.

**Phagocytosis** (fag″o-si-to′sis), meaning "cell eating," is similar to pinocytosis, but the cell takes in solids rather than liquids. Certain types of white blood cells are called *phagocytes* because they can take in solid particles such as bacteria and cellular debris. When a phagocyte first encounters a particle, the particle attaches to the phagocyte's cell membrane. This stimulates a portion of the membrane to project outward, surround the particle, and slowly draw it inside the cell. The part of the membrane surrounding the particle detaches from the cell's surface, forming a vesicle containing the particle (fig. 3.19).

Once a particle has been phagocytized by a cell, a lysosome combines with the vesicle containing the particle (phagosome) to form a phagolysosome, and

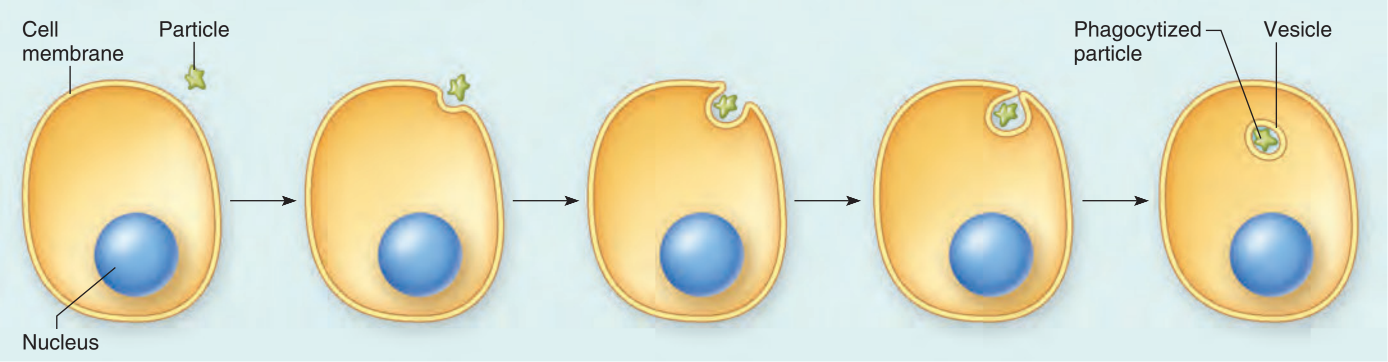


**FIGURE 3.19** APR A cell may use phagocytosis to take in a solid particle from its surroundings.

digestive enzymes decompose the contents. The products of this decomposition then leave the phagolysosome and enter the cytoplasm. Exocytosis may expel any remaining residue.

Pinocytosis and phagocytosis engulf any molecules in the vicinity of the cell membrane. In contrast, **receptor-mediated endocytosis** moves very specific kinds of particles into the cell. In this process, protein molecules extend through the cell membrane to the outer surface, where they form receptors to which only specific molecules from outside the cell, called their *ligands,* can bind (fig. 3.20). Cholesterol molecules enter cells by receptor-mediated endocytosis. Table 3.2 summarizes the types of movements into and out of cells.

**PRACTICE**

22. Explain the mechanism that maintains unequal concentrations of ions on opposite sides of a cell membrane.
23. How are facilitated diffusion and active transport similar and different?
24. What is the difference between endocytosis and exocytosis?
25. Explain how receptor-mediated endocytosis is more specific than pinocytosis or phagocytosis.

## 3.4 | The Cell Cycle

The series of changes that a cell undergoes from the time it forms until it divides is called the *cell cycle* (fig. 3.21). This cycle may seem simple: A newly formed cell grows for a time and then divides to form two new cells, which in turn may grow and divide. Yet the phases and timing of the cycle are quite complex. The major phases are interphase, mitosis, and cytoplasmic division (cytokinesis). Then the resulting "daughter" cells may undergo further changes that make them specialize. Groups of special proteins interact at certain times in the cell cycle, called *checkpoints,* in ways that control the cell cycle. Of particular importance is the restriction checkpoint that determines a cell's fate. The cell may continue in the cell cycle and divide, move into a nondividing stage as a specialized cell, or die.

The cell cycle is very precisely regulated. Stimulation from a hormone or growth factor may trigger cell division. This occurs, for example, when the breasts develop into milk-producing glands during pregnancy. Disruption of the cell cycle can affect health: If cell division is too infrequent, a wound cannot heal; if too frequent, a cancer grows. Clinical Application 3.2 discusses cancer.

Most cells do not normally divide continually. If grown in the laboratory, most types of human cells divide only forty to sixty times. Presumably, such controls operate in the body too. Some cells, such as those that line the small intestine, may divide the maximum number of times. Others, such as nerve cells, normally do not divide. A cell "knows" when to stop dividing because of a built-in "clock" in the form of the chromosome tips. These chromosome regions, called *telomeres,* shorten with each cell division. When the telomeres shorten to a certain length, the cell no longer divides. An enzyme called telomerase keeps telomeres long in cell types that must continually divide, such as certain cells in bone marrow.

Studies show that chronic psychological or emotional stress, obesity, and persistently elevated blood glucose levels can hasten telomere shortening.

### Interphase

Before a cell actively divides, it must grow and duplicate much of its contents, so that two "daughter" cells can form from one. This period of preparedness is called **interphase.**

Once thought to be a time of rest, interphase is actually a time of great synthetic activity, when the cell obtains and utilizes nutrients to manufacture new living material and maintain its routine functions. The cell duplicates membranes, ribosomes, lysosomes, and mitochondria. Perhaps most importantly, the cell in interphase takes on

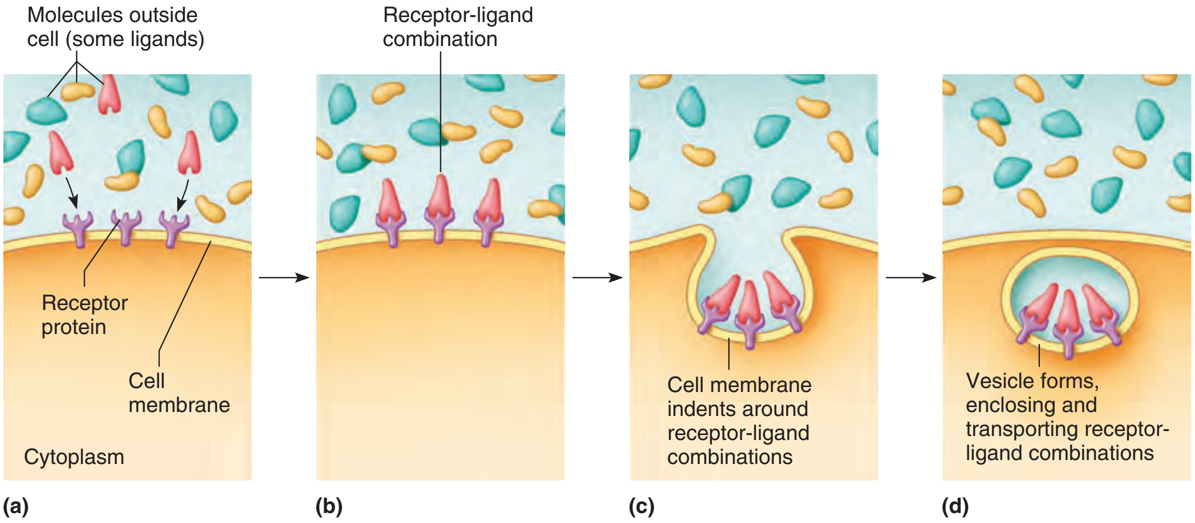

Molecules outside cell (some ligands)
Receptor protein
Cell membrane
Cytoplasm
Receptor-ligand combination
Cell membrane indents around receptor-ligand combinations
Vesicle forms, enclosing and transporting receptor-ligand combinations
(a)
(b)
(c)
(d)

**FIGURE 3.20** Receptor-mediated endocytosis brings specific molecules into a cell. **(a,b)** A specific molecule (ligand) binds to a receptor protein, forming a receptor-ligand combination. **(c)** The binding of the ligand to the receptor protein stimulates the cell membrane to indent. **(d)** Continued indentation forms a vesicle, which encloses and then transports the molecule into the cytoplasm.

**TABLE 3.2 Movements Through Cell Membranes**

| Process | Characteristics | Source of Energy | Example |
|---|---|---|---|
| **Passive mechanisms** | | | |
| Diffusion | Molecules move through the phospholipid bilayer from regions of higher concentration to regions of lower concentration. | Molecular motion | Exchange of oxygen and carbon dioxide in the lungs |
| Facilitated diffusion | Molecules move across the membrane through channels or by carrier molecules from a region of higher concentration to one of lower concentration. | Molecular motion | Movement of glucose through a cell membrane |
| Osmosis | Water molecules move through a selectively permeable membrane toward the solution with more impermeant solute (greater osmotic pressure). | Molecular motion | Distilled water entering a cell |
| Filtration | Smaller molecules are forced through porous membranes from regions of higher pressure to regions of lower pressure. | Hydrostatic pressure | Water molecules leaving blood capillaries |
| **Active mechanisms** | | | |
| Active transport | Carrier molecules transport molecules or ions through membranes from regions of lower concentration toward regions of higher concentration. | Cellular energy (ATP) | Movement of various ions, sugars, and amino acids through membranes |
| Endocytosis | | | |
| Pinocytosis | Membrane engulfs droplets containing dissolved molecules from surroundings. | Cellular energy | Intestinal absorption of dissolved nutrients |
| Phagocytosis | Membrane engulfs particles from surroundings. | Cellular energy | White blood cell engulfing bacterial cell |
| Receptor-mediated endocytosis | Membrane engulfs selected molecules combined with receptor proteins. | Cellular energy | Cell removing cholesterol molecules from its surroundings |
| Exocytosis | Vesicle fuses with membrane and releases contents outside of the cell. | Cellular energy | Neurotransmitter release |

## CLINICAL APPLICATION 3.2

## Cancer

Cancer is a group of closely related diseases that can affect many different organs. One in three of us will develop cancer. These conditions result from changes in genes (mutations) that alter the cell cycle. Cancers share the following characteristics:

1. **Hyperplasia** is uncontrolled cell division. Normal cells divide a set number of times, signaled by the shortening of chromosome tips. Cancer cells make *telomerase,* which keeps chromosome tips long and silences signals that would stop division.
2. **Dedifferentiation** is loss of the specialized structures and functions of the normal type of cell from which the cancer cells descend (fig. 3A).
3. **Invasiveness** is the ability of cancer cells to break through boundaries, called *basement membranes,* that separate cell layers.
4. **Angiogenesis** is the ability of cancer cells to induce extension of nearby blood vessels, which nourish the cells and remove wastes, enabling the cancer to grow.
5. **Metastasis** is the spread of cancer cells to other tissues, through the bloodstream or lymphatic system.

Mutations in certain genes cause cancers. Such a mutation may activate a cancer-causing oncogene (a gene that normally controls mitotic rate) or inactivate a protective gene called a tumor suppressor. A person may inherit one abnormal cancer-causing gene variant, present in all cells, and develop cancer when the second copy of that gene mutates in a cell of the organ that will be affected. This second mutation may occur in response to an environmental trigger. That is, cancer usually entails mutations in somatic (non-sex) cells.

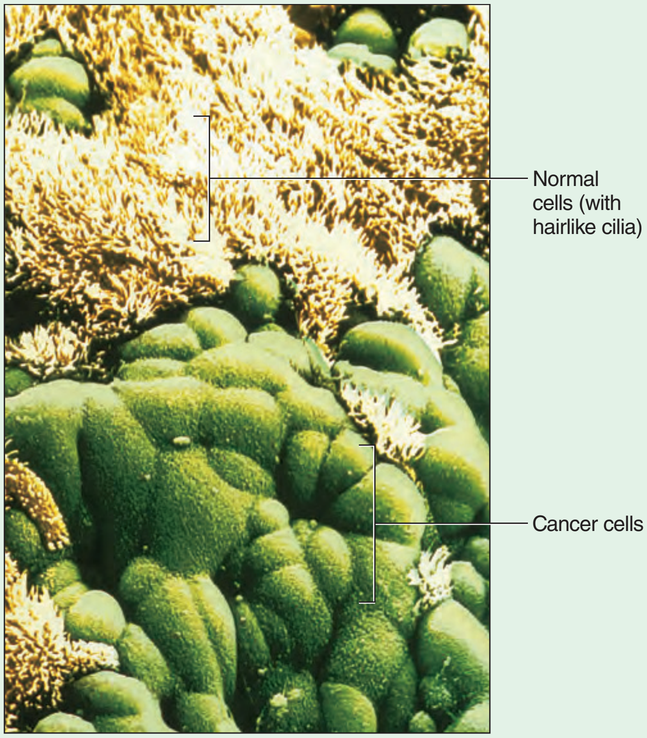

Normal cells (with hairlike cilia)
Cancer cells

**FIGURE 3A** The absence of cilia on these cancer cells, compared to the nearby cilia-fringed cells from which they arose, is one sign of their dedifferentiation (2,250×).

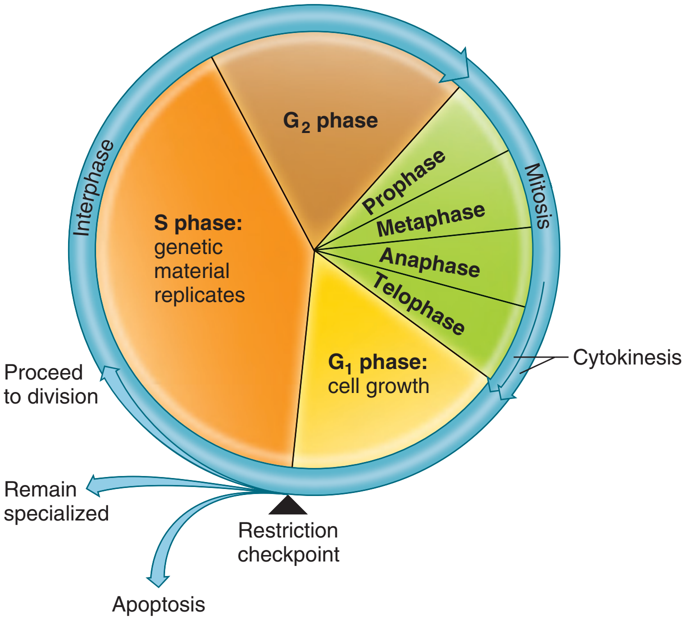

$G_2$ phase
Interphase
S phase: genetic material replicates
Prophase
Metaphase
Anaphase
Telophase
Mitosis
$G_1$ phase: cell growth
Cytokinesis
Proceed to division
Remain specialized
Restriction checkpoint
Apoptosis

**FIGURE 3.21** The cell cycle is divided into interphase, when cellular components duplicate, and cell division (mitosis and cytokinesis), when the cell splits in two, distributing its contents into two daughter cells. Interphase is divided into two gap phases ($G_1$ and $G_2$) when specific molecules and structures duplicate, and a synthesis phase (S), when the genetic material (DNA) replicates. Mitosis can be considered in stages—prophase, metaphase, anaphase, and telophase.

the tremendous task of replicating its genetic material. This is important so that each of the two new cells will have a complete set of genetic instructions.

Interphase is considered in phases. DNA is replicated during the S (or synthesis) phase, which is bracketed by two gap (or growth) periods, called $G_1$ and $G_2$, when other structures are duplicated.

## Cell Division

A cell can divide in two ways. One type of cell division is *meiosis,* which is part of *gametogenesis,* the formation of egg cells (in the female) and sperm cells (in the male). Because an egg fertilized by a sperm must have the normal complement of 46 chromosomes, both the egg and the sperm must first halve their normal chromosome number to 23 chromosomes. Meiosis, through a process called reduction division, accomplishes this. Only a few cells undergo meiosis, which is discussed in chapter 19 (pp. 520–521 and 529).

The other, much more common form of cell division increases cell number, which is necessary for growth and development and for wound healing. It consists of two separate processes: (1) division of the nucleus, called **mitosis** (mi-to′sis), and (2) division of the cytoplasm, called **cytokinesis** (si″to-ki-ne′sis).

Division of the nucleus must be very precise because it contains the DNA. Each new cell resulting from mitosis must have a complete and accurate copy of this information to survive. DNA replicates during interphase, but it is equally distributed into two cells during mitosis.

Mitosis is described in stages, but the process is actually continuous (fig. 3.22). Stages, however, indicate the sequence of major events. The stages are:

1. **Prophase** One of the first signs that a cell is going to divide is that the chromosomes become visible in the nucleus when stained. This happens because the genetic material coils very tightly, holding on to particles of stain. Because the cell has gone through S phase, each prophase chromosome is composed of two identical structures (chromatids), which are temporarily attached at a region on each called the *centromere.*

   The centrioles of the centrosome replicate just before mitosis begins. During prophase, the two newly formed centriole pairs move to opposite ends of the cell. Soon the nuclear envelope and the nucleolus break up, disperse, and are no longer visible. Microtubules are assembled from tubulin proteins in the cytoplasm and associate with the centrioles and chromosomes. A spindle-shaped array of microtubules (spindle fibers) forms between the centrioles as they move apart.
2. **Metaphase** The chromosomes line up about midway between the centrioles, as a result of microtubule activity. Spindle fibers attach to the centromeres of each chromosome so that a fiber from one pair of centrioles contacts one centromere, and a fiber from the other pair of centrioles attaches to the other centromere.
3. **Anaphase** The centromeres are pulled apart. As the chromatids separate, they become individual chromosomes that move in opposite directions, once again guided by microtubule activity. The spindle fibers shorten and pull their attached chromosomes toward the centrioles at opposite ends of the cell.
4. **Telophase** The final stage of mitosis begins when the chromosomes complete their migration toward the centrioles. It is much like the reverse of prophase. As the chromosomes approach the centrioles, they elongate and unwind from rods into threadlike chromatin. A nuclear envelope forms around each chromosome set, and nucleoli appear within the new nuclei. Finally, the microtubules disassemble into free tubulin molecules.

## Cytoplasmic Division

Cytoplasmic division (cytokinesis) begins during anaphase, when the cell membrane starts to constrict around the middle of the cell. This constriction, called a *cleavage furrow,* continues through telophase. Contraction of a ring of microfilaments, which assemble in the cytoplasm and attach to the inner surface of the cell membrane, divides the cytoplasm. The contractile ring forms at right angles to the microtubules that pulled the chromosomes to opposite sides of the cell during mitosis. The ring pinches inward, separating the two newly formed nuclei and distributing about half of the organelles into each new cell. The newly formed cells may differ slightly in size and number of organelles, but they contain identical DNA.

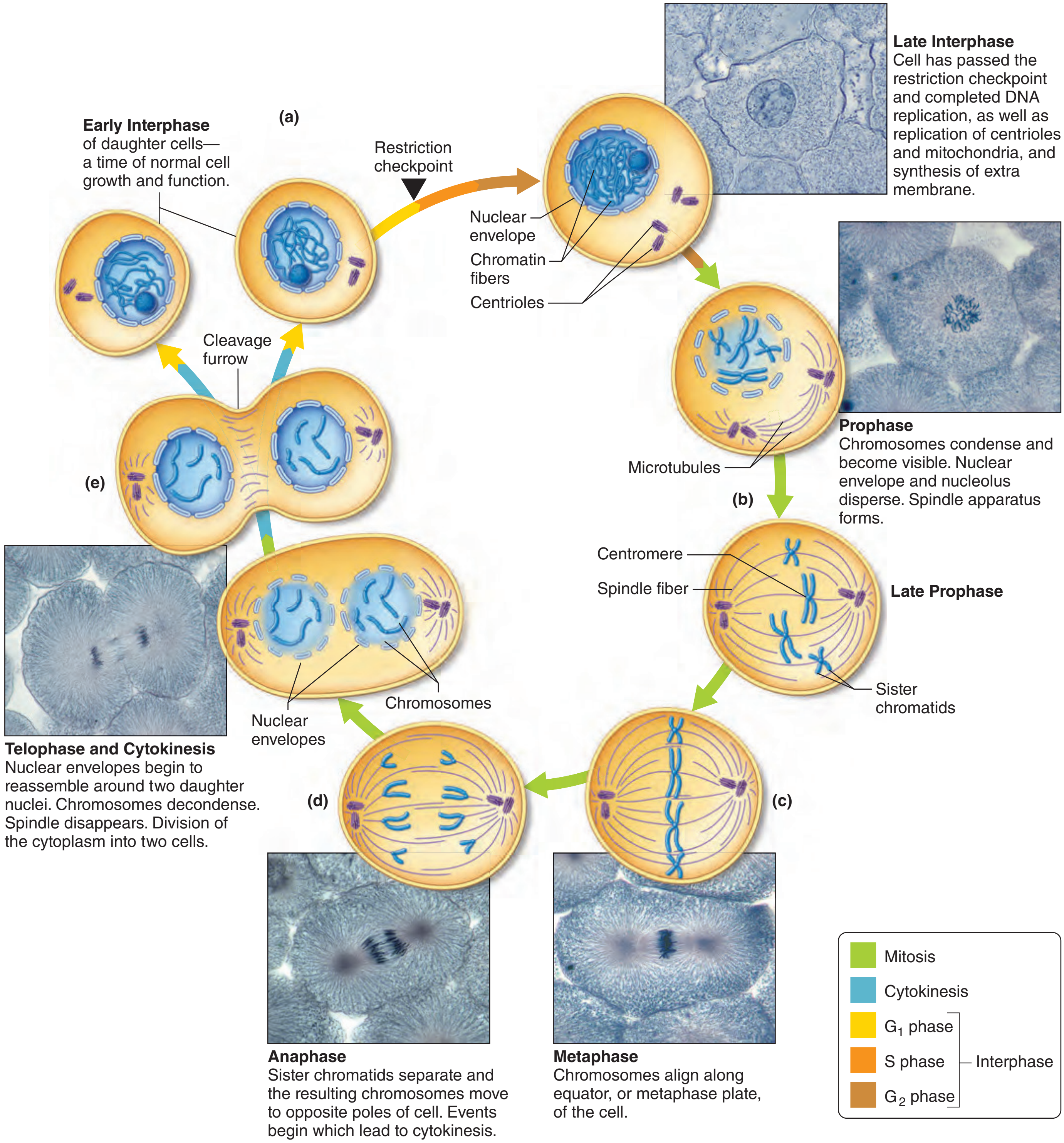
**PRACTICE**

26. Outline the cell cycle.
27. Explain regulation of the cell cycle.
28. Describe the events that occur during mitosis.

## Cell Differentiation

Cells come from preexisting cells, by the processes of mitosis and cytokinesis. Cell division explains how a fertilized egg develops into an individual consisting of trillions of cells, of at least 290 specialized types, including 14 unique to the embryo or fetus. The process of specialization is called **differentiation.**

The ability to generate new cells is essential to the growth and repair of tissues. Cells that retain the ability to divide repeatedly without specializing, called **stem cells,** allow for this continual growth and renewal. A stem cell divides mitotically to yield either two daughter cells like itself (stem cells), or one daughter cell that



**Early Interphase**
of daughter cells—
a time of normal cell
growth and function.

**Late Interphase**
Cell has passed the
restriction checkpoint
and completed DNA
replication, as well as
replication of centrioles
and mitochondria, and
synthesis of extra
membrane.

**Prophase**
Chromosomes condense and
become visible. Nuclear
envelope and nucleolus
disperse. Spindle apparatus
forms.

**Late Prophase**

**Metaphase**
Chromosomes align along
equator, or metaphase plate,
of the cell.

**Anaphase**
Sister chromatids separate and
the resulting chromosomes move
to opposite poles of cell. Events
begin which lead to cytokinesis.

**Telophase and Cytokinesis**
Nuclear envelopes begin to
reassemble around two daughter
nuclei. Chromosomes decondense.
Spindle disappears. Division of
the cytoplasm into two cells.

(a)
Restriction checkpoint
Nuclear envelope
Chromatin fibers
Centrioles
Microtubules
(b)
Centromere
Spindle fiber
Sister chromatids
(c)
(d)
Chromosomes
Nuclear envelopes
(e)
Cleavage furrow
🟩 Mitosis
🟦 Cytokinesis
🟨 $G_1$ phase
🟧 S phase
🟫 $G_2$ phase
Interphase

**FIGURE 3.22** APR Mitosis and cytokinesis produce two cells from one. **(a)** During interphase, before mitosis, chromosomes are visible only as chromatin fibers. A single pair of centrioles is present, but not visible at this magnification. **(b)** In prophase, as mitosis begins, chromosomes have condensed and are easily visible when stained. The centrioles have replicated, and each pair moves to an opposite end of the cell. The nuclear envelope and nucleolus disappear, and spindle fibers associate with the centrioles and the chromosomes. **(c)** In metaphase, the chromosomes line up midway between the centrioles. **(d)** In anaphase, the centromeres are pulled apart by the spindle fibers, and the chromatids, now individual chromosomes, move in opposite directions. **(e)** In telophase, chromosomes complete their migration and unwind to become chromatin fibers, the nuclear envelope re-forms, and microtubules disassemble. Cytokinesis, which actually began during anaphase, continues during telophase. Not all chromosomes are shown in these drawings. (Micrographs 360×)

is a stem cell and one that becomes partially specialized, termed a **progenitor cell.** The ability of a stem cell to divide and give rise to at least one other stem cell is called self-renewal. A progenitor cell's daughter cells can become any of a few cell types. For example, a neural stem cell divides to give rise to another stem cell and a neural progenitor cell. The progenitor cell then can divide, and its daughter cells differentiate, becoming nervous tissue. All of the differentiated cell types in a human body arise through such lineages of stem and progenitor cells. Figure 3.23 depicts a few of them.

Many organs have stem or progenitor cells that are stimulated to divide when injury or illness occurs. This action replaces cells, promoting healing. For example, one in 10,000 to 15,000 bone marrow cells is a stem cell, which can give rise to blood cells as well as several other cell types. Stem cells in organs may have been set aside in the embryo or fetus as repositories of future healing. Certain stem cells can travel to replace injured or dead cells in response to signals sent from the site of damage.

Throughout development, cells progressively specialize by utilizing different parts of the complete genetic instructions, or genome, that are present in each cell. That is, some genes are "turned on" in certain cells, and other genes are turned on in other cell types. In this way, for example, an immature bone cell forms from a progenitor cell by synthesizing proteins that bind bone mineral and an enzyme required for bone formation. An immature muscle cell, in contrast, forms from a muscle progenitor cell by synthesizing contractile proteins. The bone progenitor does not produce contractile proteins, nor does the muscle progenitor produce mineral-binding proteins. The final differentiated cell is like a database from which only some information is accessed.

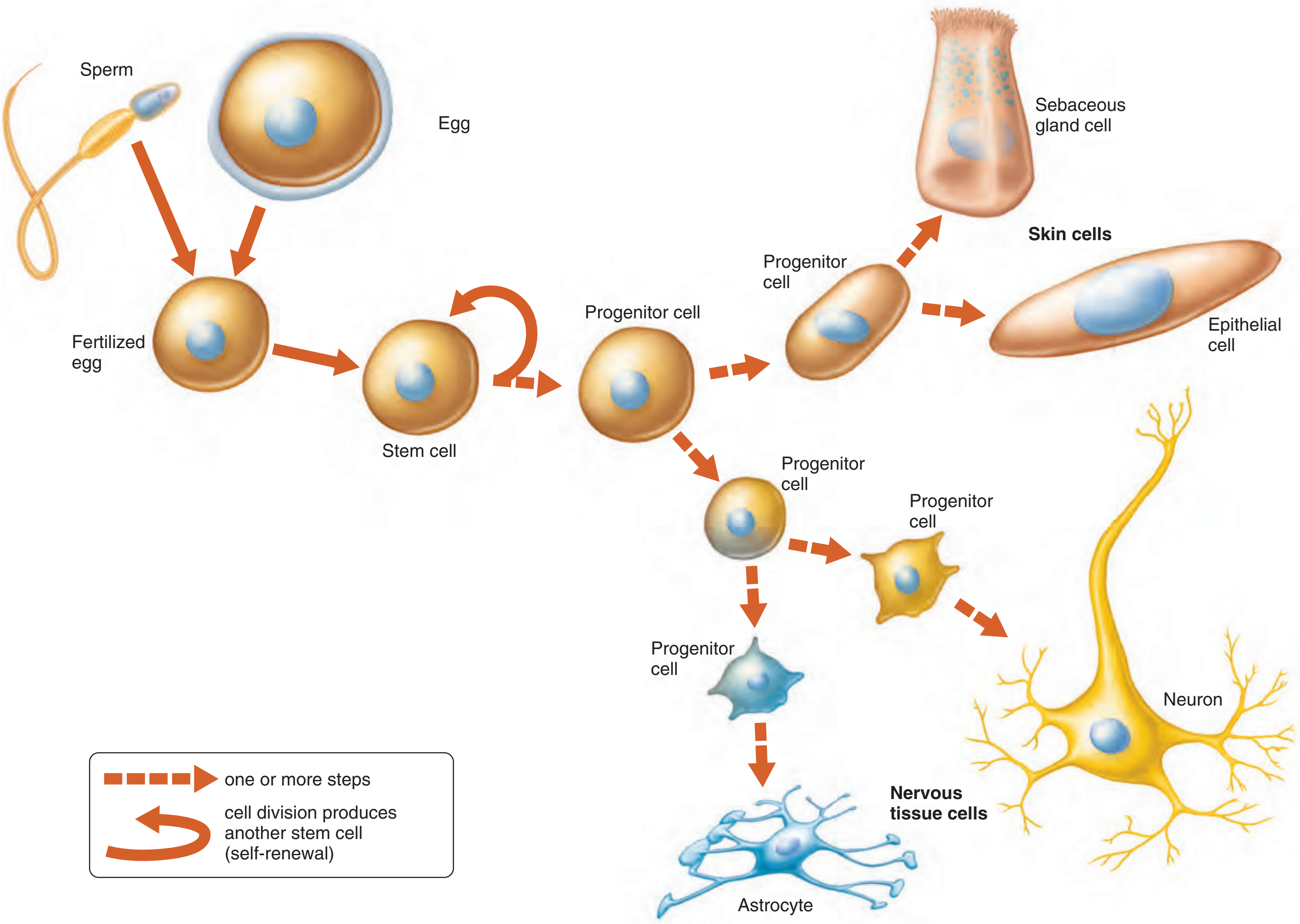

Sperm
Egg
Fertilized egg
Stem cell
Progenitor cell
Progenitor cell
Sebaceous gland cell
Skin cells
Epithelial cell
Progenitor cell
Progenitor cell
Progenitor cell
Neuron
Nervous tissue cells
Astrocyte
one or more steps
cell division produces another stem cell (self-renewal)

**FIGURE 3.23** Cells specialize along cell lineage pathways. All cells in the human body ultimately descend from stem cells, through the processes of mitosis and differentiation. This simplified view depicts a few of the pathways that cells follow, grouping the cell types by the closeness of their lineages. Imagine the complexity of the lineages of the more than 260 human cell types!

## Cell Death

A cell that does not divide or specialize has another option—it may die. **Apoptosis** (ap″o-to′sis) is a form of cell death that is a normal part of development, rather than the result of injury or disease. Apoptosis sculpts organs from naturally overgrown tissues. In the fetus, for example, apoptosis carves away webbing between developing fingers and toes, removes extra brain cells, and preserves only those immune system cells that recognize the body's cell surfaces. After birth, apoptosis occurs after a sunburn—it peels away damaged skin cells that might otherwise turn cancerous.

A cell in the throes of apoptosis goes through characteristic steps. It rounds up and bulges, the nuclear membrane breaks down, chromatin condenses, and enzymes cut the chromosomes into many equal-size pieces of DNA. Finally, the cell shatters into membrane-enclosed fragments, and a scavenger cell engulfs and destroys them. Apoptosis is a little like cleaning up a very messy room by placing garbage in many garbage bags, which are then removed.

### PRACTICE

29. Why must cells divide and specialize?
30. Distinguish between a stem cell and a progenitor cell.
31. How are new cells generated and how do they specialize?
32. How is cell death a normal part of development?

## Summary Outline

### 3.1 Introduction (p. 61)

*Cells vary considerably in size, shape, and function. The shapes of cells make possible their functions.*

### 3.2 Composite Cell (p. 61)

*A cell includes a cell membrane, cytoplasm, and a nucleus. Organelles perform specific functions. The nucleus controls overall cell activities because it contains DNA, the genetic material.*

1. Cell membrane
   a. The cell membrane forms the outermost limit of the living material.
   b. It is a selectively permeable passageway that controls the entrance and exit of substances. Its molecules transmit signals.
   c. The cell membrane includes protein, lipid, and carbohydrate molecules.
   d. The cell membrane's framework is mainly a bilayer of phospholipid molecules.
   e. Molecules that are soluble in lipids pass through the cell membrane easily, but water-soluble molecules do not.
   f. Proteins function as receptors on membrane surfaces and form channels for the passage of ions and molecules.
   g. Patterns of surface carbohydrates associated with membrane proteins enable certain cells to recognize one another.
2. Cytoplasm
   a. Cytoplasm contains networks of membranes, organelles, and the rods and tubules of the cytoskeleton, suspended in cytosol.
   b. The endoplasmic reticulum is a tubular communication system in the cytoplasm that transports lipids and proteins.
   c. Ribosomes function in protein synthesis.
   d. The Golgi apparatus adds sugars to certain proteins and processes them for secretion.
   e. Mitochondria contain enzymes that catalyze reactions that release energy from nutrient molecules.
   f. Lysosomes contain digestive enzymes that decompose substances.
   g. Peroxisomes house enzymes that catalyze breakdown of hydrogen peroxide and fatty acids, and detoxification of alcohol.
   h. Microfilaments (actin) and microtubules (tubulin) aid cellular movements and support and stabilize the cytoplasm and organelles. Together they form the cytoskeleton. Microtubules also form centrioles, cilia, and flagella.
   i. The centrosome contains centrioles that aid in distributing chromosomes during cell division.
   j. Cilia and flagella are motile extensions from cell surfaces.
   k. Vesicles transport substances within and between cells.
3. Cell nucleus
   a. The nucleus is enclosed in a double-layered nuclear envelope.
   b. It contains a nucleolus, where ribosomes are produced.
   c. It contains chromatin, which is composed of loosely coiled fibers of DNA and protein. As chromatin fibers condense during cell division, chromosomes hold stain and can be visualized using a microscope.

### 3.3 Movements Through Cell Membranes (p. 70)

*The cell membrane is a barrier through which substances enter and leave a cell.*

1. Passive transport mechanisms do not require cellular energy.
   a. Diffusion
      (1) Diffusion is the movement of molecules or ions from regions of higher concentration to regions of lower concentration.
      (2) In the body, diffusion exchanges oxygen and carbon dioxide.
   b. Facilitated diffusion
      (1) In facilitated diffusion, ion channels and special carrier molecules move substances through the cell membrane.
      (2) This process moves substances only from regions of higher concentration to regions of lower concentration.
   c. Osmosis
      (1) Osmosis is the movement of water across a selectively permeable membrane into a compartment containing solute that cannot cross the same membrane.
      (2) Osmotic pressure increases as the number of impermeant particles dissolved in a solution increases.
      (3) A solution is isotonic to a cell when it has the same osmotic pressure as the cell.
      (4) Cells lose water when placed in hypertonic solutions and gain water when placed in hypotonic solutions.

   d. Filtration
      (1) Filtration is the movement of molecules through membranes from regions of higher hydrostatic pressure to regions of lower hydrostatic pressure.
      (2) Blood pressure causes filtration through porous capillary walls, forming tissue fluid.
2. Active mechanisms require cellular energy.
   a. Active transport
      (1) Active transport moves particles through membranes from a region of lower concentration to a region of higher concentration.
      (2) It requires cellular energy from ATP and carrier molecules in the cell membrane.
   b. Endocytosis and exocytosis
      (1) Endocytosis conveys large particles into a cell. Exocytosis is the reverse of endocytosis.
      (2) In pinocytosis, a cell membrane engulfs droplets of liquid.
      (3) In phagocytosis, a cell membrane engulfs solid particles.
      (4) Receptor-mediated endocytosis moves specific types of particles into cells.

### 3.4 The Cell Cycle (p. 77)

*The cell cycle includes interphase, mitosis, and cytoplasmic division. It is highly regulated.*

1. Interphase
   a. During interphase, a cell duplicates membranes, ribosomes, organelles, and DNA.
   b. Interphase terminates when mitosis begins.
2. Cell Division
   a. Meiosis is a form of cell division that forms sex cells.
   b. Mitosis is the division and distribution of complete sets of genetic material to new cells, increasing cell number.
   c. The stages of mitosis are prophase, metaphase, anaphase, and telophase.
3. Cytoplasmic division distributes cytoplasm into two portions, completing about the same time as mitosis.
4. Differentiation is cell specialization. Stem cells provide new cells for growth and repair. They give rise to other stem cells and to progenitor cells that begin to specialize. Differentiation reflects the activation of specific sets of genes.
5. A cell that does not divide or differentiate may undergo apoptosis, a form of cell death that is a normal part of development.

## CHAPTER ASSESSMENTS

### 3.1 Introduction

**1.** An adult human body consists of about __________ cells. (p. 61)
   a. 2 billion
   b. 50 billion
   c. 75 trillion
   d. 8 quadrillion

**2.** Define *cell.* (p. 61)

**3.** Discuss how cells differ from one another. (p. 61)

### 3.2 Composite Cell

**4.** The three major parts of a cell are __________. (p. 61)
   a. the nucleus, the nucleolus, and the nuclear envelope
   b. the nucleus, cytoplasm, and the cell membrane
   c. a nerve cell, an epithelial cell, and a muscle cell
   d. endoplasmic reticulum, Golgi apparatus, and ribosomes

**5.** Explain the general function of organelles. (p. 62)

**6.** Define *selectively permeable.* (p. 62)

**7.** Describe the structure of a cell membrane and explain how this structural organization provides the membrane's function. (p. 62)

**8.** List three functions of membrane proteins. (p. 64)

**9.** Match the following structures with their definitions: (pp. 65–68)

   (1) Golgi apparatus
   (2) mitochondria
   (3) peroxisomes
   (4) cilia
   (5) endoplasmic reticulum
   (6) cytoskeleton
   (7) vesicles
   (8) ribosomes

   A. sacs that contain enzymes that catalyze a variety of specific biochemical reactions
   B. structures on which protein synthesis occurs
   C. structures that house the reactions that release energy from nutrients
   D. a network of microfilaments and microtubules that supports and shapes a cell
   E. a structure that adds sugars to certain proteins and processes them for secretion
   F. membrane-bounded sacs
   G. a network of membranous channels and sacs where lipids and proteins are synthesized
   H. hairlike structures that extend from certain cell surfaces and wave about

**10.** List the parts of the nucleus and explain why each is important. (p. 69)

### 3.3 Movements Through Cell Membranes

**11.** Distinguish between active and passive mechanisms of movement across cell membranes. (p. 70)

**12.** Match the transport mechanisms with their descriptions. (pp. 70–76)

   (1) diffusion
   (2) facilitated diffusion
   (3) filtration
   (4) active transport
   (5) endocytosis
   (6) exocytosis

   A. the cell membrane engulfs a particle or substance, drawing it into the cell in a vesicle
   B. movement down the concentration gradient with a carrier protein, without energy input
   C. movement down the concentration gradient without a carrier protein or energy input
   D. a particle or substance leaves a cell in a vesicle that merges with the cell membrane
   E. movement against the concentration gradient with energy input
   F. hydrostatic pressure forces substances through membranes

**13.** Define *osmosis.* (p. 73)

**14.** Distinguish among hypertonic, hypotonic, and isotonic solutions. (p. 74)

**15.** Explain how phagocytosis differs from receptor-mediated endocytosis. (p. 76)

### 3.4 The Cell Cycle

**16.** Explain why it is important for the body to regulate the cell cycle. (p. 77)

**17.** Distinguish between interphase and mitosis. (p. 80)

**18.** The period of the cell cycle when DNA replicates is _____. (p. 80)
   a. $G_1$ phase
   b. $G_2$ phase
   c. S phase
   d. prophase

**19.** Explain how meiosis differs from mitosis. (p. 80)

**20.** ___________ occur simultaneously. (p. 80)
   a. $G_1$ phase and $G_2$ phase
   b. Interphase and mitosis
   c. Cytokinesis and telophase
   d. Prophase and metaphase

**21.** Describe the events of mitosis in sequence. (p. 80)

**22.** Define *differentiation.* (p. 80)

**23.** A stem cell ___________. (p. 80)
   a. forms from a progenitor cell
   b. self-renews
   c. is differentiated
   d. gives rise to only fully differentiated daughter cells

**24.** Describe the steps of apoptosis. (p. 83)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOME 3.2

1. Why does a muscle cell contain many mitochondria, and why does a white blood cell contain many lysosomes?
2. Organelles compartmentalize a cell, much as a department store displays related items together. What advantage does such compartmentalization offer a large cell? Cite two examples of organelles and the activities they compartmentalize.
3. Exposure to tobacco smoke immobilizes cilia, and they eventually disappear. How might this effect explain why smokers have an increased incidence of coughing and respiratory infections?

### OUTCOME 3.3

4. Which process—diffusion, osmosis, or filtration—is utilized in the following situations?
   a. Injection of a drug that is hypertonic to the tissues stimulates pain.
   b. The urea concentration in the dialyzing fluid of an artificial kidney is decreased.
5. What characteristic of cell membranes may explain why fat-soluble substances such as chloroform and ether rapidly affect cells?

### OUTCOME 3.4

6. New treatments for several conditions are being developed using stem cells in medical waste, such as biopsy material, teeth, menstrual blood, umbilical cords, and fatty tissue removed in liposuction. For example, fat samples from injured horses are used to grow stem cells to treat tendon injuries. Explain how the two defining characteristics of stem cells enable them to be used to replace damaged or diseased tissue, so that the new tissue functions as opposed to forming a scar.
7. Explain how the cell cycle of a cancer cell is abnormal.

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# 4

# Cellular Metabolism

*Chronic exposure to arsenic in drinking water causes the burning, colored lesions of arsenicosis.*

**A**rsenic poisoning. Disrupting the body's ability to extract energy from nutrients can have serious effects on health. Arsenic is a chemical element that, if present in the body in excess, shuts down metabolism. It can do so suddenly or gradually.

Given in one large dose, arsenic causes chest pain, vomiting, diarrhea, shock, coma, and death. In contrast, a series of many small doses causes dark skin lesions that feel as if they are burning, numb hands and feet, and skin cancer. The condition may progress to paralysis and organ failure. Such gradual poisoning, called arsenicosis, may occur from contact with pesticides or environmental pollutants. The world's largest outbreak of arsenicosis, however, is due to a natural exposure.

When the World Bank and UNICEF began tapping into aquifers in India and Bangladesh in the late 1960s, they were trying to supply clean water to areas ravaged by sewage and industrial waste released from rivers subject to cycles of floods and droughts. Millions of people had already perished from diarrheal diseases due to the poor sanitation. But digging wells to provide clean water backfired when workers unwittingly penetrated a layer of sediment naturally rich in arsenic. The chemical has been leaching into the water in at least 2 million wells in Bangladesh alone ever since, reaching levels 30 times the safety limit set by the World Health Organization. Effects on health took several years to show up. When they did, the people thought arsenicosis was contagious. In addition to their physical pain, affected individuals bore the psychological pain of being shunned.

Arsenic damages the body by binding to bonds between sulfur atoms in proteins. The effects on metabolism largely stem from impairment of an enzyme that helps the breakdown products of glucose enter the mitochondria, where energy is extracted. Cells run out of energy.

Today UNICEF is helping the people of India and Bangladesh avoid arsenic poisoning. They are diagnosing and treating arsenicosis, and providing tanks to store rainwater. A vast education campaign has done much to quell the stigma of arsenicosis. One program in West Bengal teaches women and teens how to recognize arsenic-tainted sediments and gives the people kits to test the water in new wells being drilled.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

**4.1 Introduction**

1. Explain the overall function of metabolism. (p. 87)

**4.2 Metabolic Reactions**

2. Compare and contrast anabolism and catabolism. (p. 87)

**4.3 Control of Metabolic Reactions**

3. Describe how enzymes control metabolic reactions. (p. 88)
4. Describe a metabolic pathway. (p. 89)

**4.4 Energy for Metabolic Reactions**

5. Identify the source of biological energy. (p. 91)
6. Describe how energy in the form of ATP becomes available for cellular activities. (p. 91)
7. Explain how cellular respiration releases chemical energy. (p. 91)

**4.5 DNA (Deoxyribonucleic Acid)**

8. Describe how DNA molecules store genetic information. (p. 94)
9. Describe how DNA molecules are replicated. (p. 94)

**4.6 Protein Synthesis**

10. Describe the steps of protein synthesis. (p. 96)

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## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**an-** [without] *an*aerobic respiration: Respiratory process that does not require oxygen.

**ana-** [up] *ana*bolism: Cellular processes that build larger molecules from smaller ones.

**cata-** [down] *cata*bolism: Cellular processes that break larger molecules into smaller ones.

**mut-** [change] *mut*ation: Change in genetic information.

**-zym** [causing to ferment] en*zym*e: Protein that speeds a chemical reaction without itself being consumed.

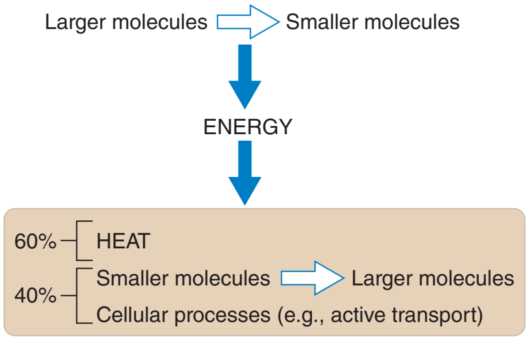
## 4.1 | Introduction

A cell is a very busy place. Thousands of chemical reactions occur inside cells to carry on the activities of life, and also to provide the specialized characteristics of different cell types. A constant energy supply is required to fuel all of this activity. In addition to energy, a cell requires information—the instruction manual of DNA, the genetic material.

Cellular metabolism is the set of chemical reactions that acquire, store, and release energy in cells. The energy comes from the chemical bonds of nutrient molecules from the diet. A cell uses some of that energy to copy DNA when the cell divides and uses energy to access genetic information to construct proteins from amino acid building blocks. Special proteins called **enzymes** (en′zīmz) are vital to all of these activities. They control each of the interrelated reactions of metabolism.

## 4.2 | Metabolic Reactions

The metabolic reactions that control a cell's use of energy are of two major types. The reactions of **anabolism** (an″ah-bol′izm) build up (synthesize) larger molecules from smaller ones, requiring input of energy. The reactions of **catabolism** (kă-tab′o-lizm) break down (decompose) larger molecules into smaller ones, releasing energy. The reactions of anabolism and catabolism together, constitute **metabolism** (mĕ-tab′o-lizm).



### Anabolism

Anabolism provides the biochemicals required for cell growth and repair. An anabolic reaction called **dehydration synthesis** (de″hi-dra′shun sin′the-sis), for example, joins many simple sugar molecules (monosaccharides) to form larger molecules of glycogen. When monosaccharides join, an —OH (hydroxyl group) from one monosaccharide molecule and an —H (hydrogen atom) from an —OH group of another are removed. As the —H and —OH react to produce a water molecule

### CAREER CORNER

### Personal Trainer

The 45-year-old man's physician advised him to start an exercise program to lose weight, so the man joined a gym. But he hadn't been to one in many years, and the rows of machines looked daunting. So he hired a personal trainer to develop an exercise routine that would be just what the doctor ordered.

A personal trainer assesses a client's fitness level and guides the client in the use of specific machines and doing mat exercises. The trainer offers advice on which weight-lifting machines to use, how many repetitions to begin with, and how often to increase repetitions. The trainer might advise the client to lift weights only every other day, so that muscles will have time to recover from the microscopic tears caused by weight lifting. Using a mat, a trainer might lead a client through a series of exercises to strengthen the core abdominal muscles.

The personal trainer is part coach, part cheerleader, encouraging exercisers to push their limits. Trainers work in athletic clubs, at corporate fitness centers, in senior centers, and at other types of facilities that have exercise equipment. Some personal trainers even train clients at their homes.

Minimal requirements to become a personal trainer include a high school diploma, cardiopulmonary resuscitation (CPR) training, and completion of a personal trainer course, which generally takes from a few months to a year. Passing a certification exam is required. Personal trainers tend to be outgoing, friendly people who enjoy helping others become physically fit.

($H_2O$), the monosaccharides are joined by a shared oxygen atom (fig. 4.1). This process repeats and the molecular chain extends.

Dehydration synthesis also links glycerol and fatty acid molecules in fat (adipose) cells to form fat molecules (triglycerides). In this case, three hydrogen atoms are removed from a glycerol molecule, and an —OH group is removed from each of three fatty acid molecules (fig. 4.2). The result is three water molecules and a single fat molecule. Shared oxygen atoms bind the glycerol and fatty acid portions.

In cells, dehydration synthesis joins amino acid molecules, forming protein molecules. When two amino acid molecules unite, an —OH from one and an —H from the —$NH_2$ group of another are removed. A water molecule forms, and the amino acid molecules are joined by a bond between a carbon atom and a nitrogen atom, called a *peptide bond* (fig. 4.3). Two bound amino acids form a *dipeptide,* and many linked in a chain form a *polypeptide.* Generally, a polypeptide that has a specific function and consists of 100 or more amino acids is considered a *protein.* Some protein molecules consist of more than one polypeptide.

Nucleic acids are also formed by dehydration synthesis joining nucleotides. This process is described later in the chapter.

## Catabolism

Catabolic reactions break down larger molecules into smaller ones. An example of a catabolic reaction is **hydrolysis** (hi-drol′ĭ-sis), which breaks down carbohydrates, lipids, and proteins, and splits a water molecule in the process. For instance, hydrolysis of a disaccharide such as sucrose yields two monosaccharides (glucose and fructose) as a molecule of water splits:

$$\underset{\text{(Sucrose)}}{C_{12}H_{22}O_{11}} + \underset{\text{(Water)}}{H_2O} \longrightarrow \underset{\text{(Glucose)}}{C_6H_{12}O_6} + \underset{\text{(Fructose)}}{C_6H_{12}O_6}$$

In this case, the bond between the simple sugars that form sucrose breaks. Then, the water supplies a hydrogen atom to one sugar and a hydroxide group to the other. Hydrolysis is the opposite of dehydration synthesis (see figs. 4.1, 4.2, and 4.3). Each of these reactions is reversible and can be summarized as follows:

$$\text{Disaccharide} + \text{Water} \underset{\longleftarrow \text{ Dehydration synthesis}}{\overset{\text{Hydrolysis} \longrightarrow}{\rightleftarrows}} \text{Monosaccharide} + \text{Monosaccharide}$$

Hydrolysis is responsible for digestion. Specifically, it breaks down carbohydrates into monosaccharides, fats into glycerol and fatty acids, proteins into amino acids, and nucleic acids into nucleotides. (Chapter 15, pages 418–432, discusses digestion in detail.)

### PRACTICE

1. What are the general functions of anabolism and catabolism?
2. What are the products of the anabolism of monosaccharides, glycerol and fatty acids, and amino acids?
3. Distinguish between dehydration synthesis and hydrolysis.

## 4.3 | Control of Metabolic Reactions

Specialized cells, such as nerve, muscle, or blood cells, carry out distinctive chemical reactions. However, all cells perform certain basic chemical reactions, such as buildup and breakdown of carbohydrates, lipids, proteins, and nucleic acids. These reactions include hundreds of specific chemical changes that occur rapidly—yet in a coordinated fashion—thanks to **enzymes**.

## Enzyme Action

Metabolic reactions require energy to proceed, as do all chemical reactions. The temperature conditions in cells, however, usually do not enable chemical reactions to proceed fast enough to support life. Enzymes make these reactions possible by lowering the amount of energy, called the *activation energy,* required to start these reactions. In this way, enzymes speed metabolic reactions. This acceleration is called *catalysis,* and an

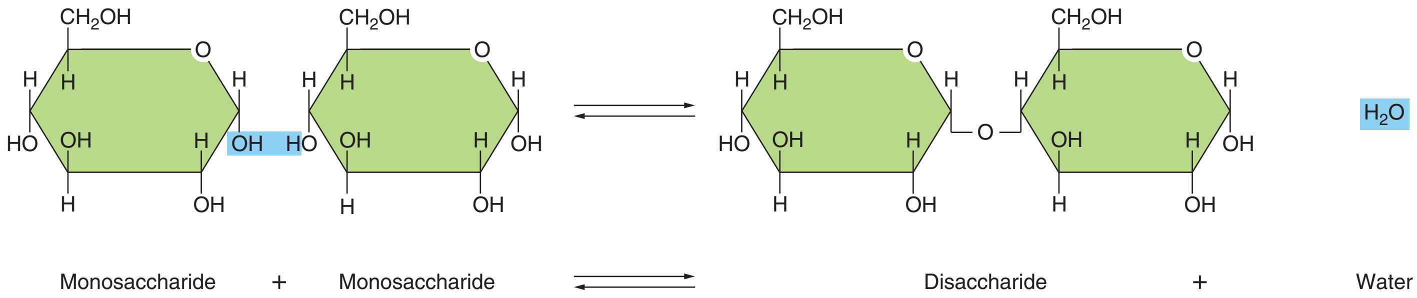


**FIGURE 4.1** Building up and breaking down molecules. A disaccharide is formed from two monosaccharides in a dehydration synthesis reaction (arrows pointing to the right). In the reverse reaction, hydrolysis, a disaccharide is broken down into two monosaccharides (arrows pointing to the left).

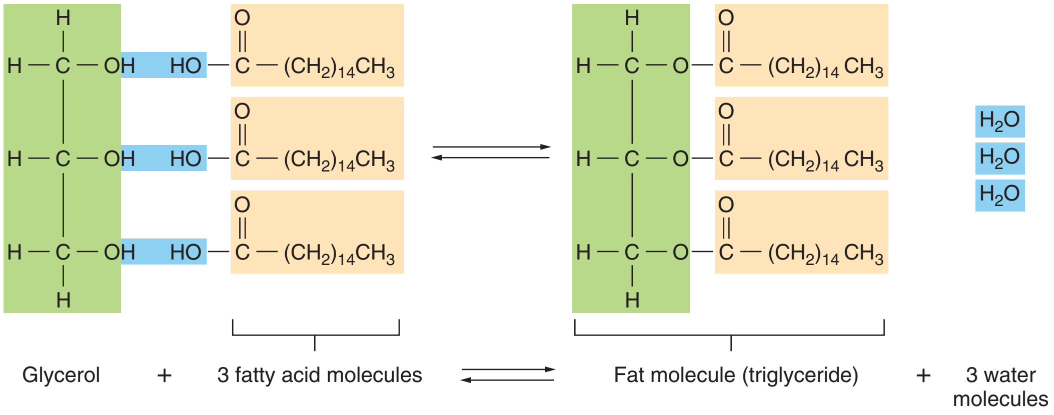


**FIGURE 4.2** Forming a fat. A glycerol molecule and three fatty acid molecules react, yielding a fat molecule (triglyceride) in a dehydration synthesis reaction (arrows pointing to the right). In the reverse reaction, hydrolysis, a triglyceride is broken down into three fatty acids and a glycerol (arrows pointing to the left).

enzyme is a catalyst. Enzyme molecules are not consumed in the reactions they catalyze and can function repeatedly. Therefore, a few enzyme molecules can have a powerful effect.

Each type of enzyme is specific, acting only on a particular type of molecule, called its **substrate** (sub′strāt). Many enzymes are named after their substrates, with *-ase* as a suffix. A lipase, for example, catalyzes a reaction that breaks down a lipid. Another example of an enzyme is *catalase*. Its substrate is hydrogen peroxide, which is a toxic by-product of certain metabolic reactions. Catalase speeds breakdown of hydrogen peroxide into water and oxygen, preventing accumulation of hydrogen peroxide, which can damage cells.

Each enzyme must recognize its specific substrate. This ability of an enzyme to identify its substrate arises from the three-dimensional shape, or conformation, of the enzyme molecule. Each enzyme's polypeptide chain twists and coils into a unique conformation that fits the particular shape of its substrate molecule.

During an enzyme-catalyzed reaction, part of the enzyme molecule called the **active site** temporarily combines with parts of the substrate molecules, forming an enzyme-substrate complex (fig. 4.4). This interaction strains certain chemical bonds in the substrates, altering their orientation so that they require less energy to react. The reaction proceeds, product forms, and the enzyme is released in its original conformation, able to bind another substrate molecule.

Many enzyme-catalyzed reactions are reversible, and in some cases the same enzyme catalyzes the reaction in both directions. An enzyme-catalyzed reaction can be summarized as follows:

**Substrate molecules** + **Enzyme molecule** → **Enzyme-substrate complex** → **Product (changed substrates)** + **Enzyme molecule**

The rate of an enzyme-catalyzed reaction depends partly on the number of enzyme and substrate molecules in the cell. A reaction is faster if the concentrations of the enzyme or the substrate increase. Enzyme efficiency varies greatly. Some enzymes can catalyze only a few reactions per second, whereas others can catalyze hundreds of thousands.

## PRACTICE

4. What is an *enzyme?*
5. How does an enzyme recognize its substrate?
6. List factors that affect the rate of an enzyme-controlled reaction.

## Enzymes and Metabolic Pathways

Specific enzymes catalyze each of the hundreds of different chemical reactions that constitute cellular metabolism. Sequences of enzyme-controlled reactions, called **metabolic pathways**, lead to synthesis or breakdown of particular biochemicals (fig. 4.5). Every cell contains hundreds of different types of enzymes.

For some pathways, the enzymes are positioned in a cell in the exact sequence as that of the reactions

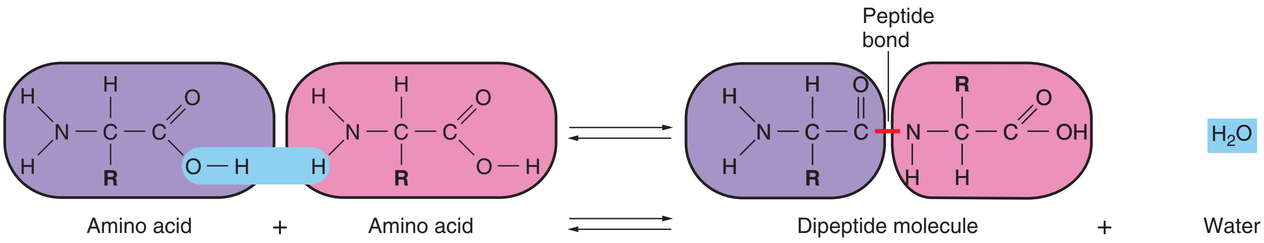


**FIGURE 4.3** Peptide bonds link amino acids. When dehydration synthesis unites two amino acid molecules, a peptide bond forms between a carbon atom and a nitrogen atom, resulting in a dipeptide molecule (arrows pointing to the right). In the reverse reaction, hydrolysis, a dipeptide molecule is broken down into two amino acids (arrows pointing to the left).

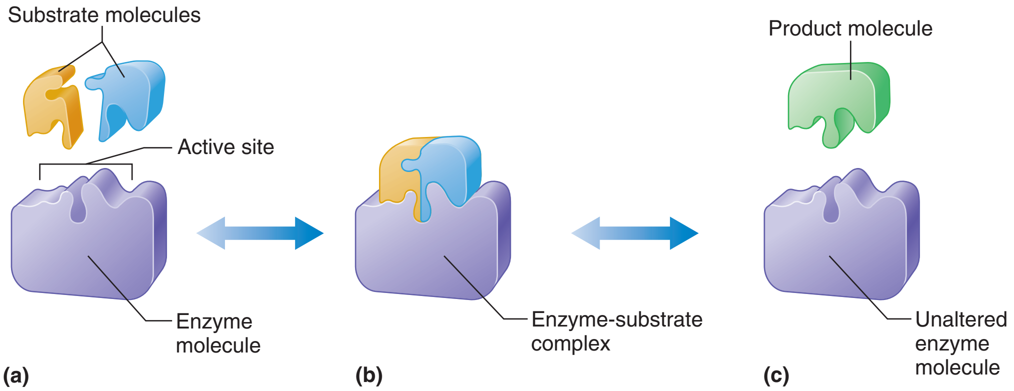


**FIGURE 4.4** APR As depicted here, many enzyme-catalyzed reactions are reversible. In the forward reaction (dark-shaded arrows), **(a)** the shapes of the substrate molecules fit the shape of the enzyme's active site. **(b)** When the substrate molecules temporarily combine with the enzyme, a chemical reaction proceeds. **(c)** The result is a product molecule and an unaltered enzyme. The active site changes shape as the substrate binds, such that formation of the enzyme-substrate complex is more like a hand fitting into a glove, which has some flexibility, than a key fitting into a lock.

they control. The rate of a metabolic pathway is often determined by a *regulatory enzyme* that catalyzes one of its steps. The number of molecules of a regulatory molecule is limited. Consequently, the enzymes can become saturated if the substrate concentration exceeds a certain level. Once the enzyme is saturated, increasing the number of substrate molecules no longer affects the reaction rate.

A regulatory enzyme that controls the entire pathway is called a *rate-limiting enzyme*, and it is generally the first enzyme in a series. This position is important because if an enzyme at some other point in the sequence were rate-limiting, an intermediate chemical in the pathway might accumulate.

### Factors That Alter Enzymes

Some enzymes become active only when they combine with a nonprotein component called a **cofactor.** It may be an ion of an element, such as copper, iron, or zinc, or a small organic molecule, called a **coenzyme** (ko-en′zīm). Many coenzymes are or are similar to vitamin molecules. An example of a coenzyme is coenzyme A, which takes part in cellular respiration, discussed in section 4.4 (p. 91).

Almost all enzymes are proteins, and like other proteins, exposure to heat, radiation, electricity, certain chemicals, or fluids with extreme pH values can denature them. Some enzymes become inactive at 45°C (113°F). Some poisons denature enzymes. Cyanide, for instance, denatures respiratory enzymes, preventing cells from releasing energy from nutrients.

### PRACTICE

7. What is a *metabolic pathway?*
8. What is a rate-limiting enzyme?
9. What does a cofactor do?
10. List factors that can denature enzymes.

## 4.4 | Energy for Metabolic Reactions

**Energy** is the capacity to change something; it is the ability to do work. We recognize energy by what it can do. Common forms of energy are heat, light, sound, electrical energy, mechanical energy, and chemical energy. Most metabolic reactions use chemical energy.

### Release of Chemical Energy

Chemical energy is held in the bonds between the atoms of molecules and is released when these bonds break. Burning is an example of an intervention that can break the bonds of chemicals in the environment (outside the body). Burning begins by applying heat. As the chemical burns, bonds break, and energy escapes as heat and light.

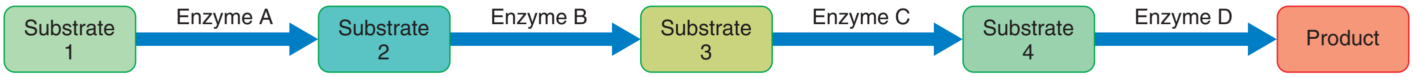


**FIGURE 4.5** A metabolic pathway consists of a series of enzyme-controlled reactions leading to formation of a product.

Cells "burn" glucose molecules in a process called **oxidation** (ok″sĭ-da′shun). The energy released from breaking the bonds of glucose powers the anabolic reactions of cells that build molecules. However, oxidation inside cells and burning outside of cells differ. Burning requires a large input of energy, most of which escapes as heat or light. In cells, enzymes reduce the activation energy required for the oxidation that occurs in the reactions of *cellular respiration*. These reactions release the energy in the bonds of nutrient molecules. Cells can capture about 40% of the energy released from breaking chemical bonds in cellular respiration and transfer it to high-energy electrons that the cell can use to synthesize molecules of **ATP (adenosine triphosphate)**. The rest of the liberated energy escapes as heat, which helps maintain body temperature.

## ATP Molecules

Each ATP molecule includes a chain of three chemical groups called phosphates (fig. 4.6). As energy is released during cellular respiration, some of it is captured in the bond of the end phosphate. When energy is required for a metabolic reaction, this terminal phosphate bond breaks, releasing the stored energy. (The second phosphate bond is high-energy too.) The cell uses ATP for a variety of functions, including active transport and synthesis of various compounds (anabolism).

An ATP molecule that has lost its terminal phosphate becomes an ADP (adenosine diphosphate) molecule. The ADP can be converted back into ATP by the addition of energy and a third phosphate. Thus, as figure 4.7 shows, ATP and ADP molecules shuttle back and forth between the energy-releasing reactions of cellular respiration and the energy-utilizing reactions of the cell.

**PRACTICE**

11. Define *energy*.
12. Explain how oxidation inside cells differs from burning in the outside environment.
13. What is the general function of ATP in metabolism?

## Cellular Respiration

Cellular respiration consists of three distinct, yet interconnected, series of reactions: *glycolysis*, the *citric acid cycle,* and the *electron transport chain*. Glycolysis and the electron transport chain are pathways, similar to figure 4.5. Figure 4.8 shows how a metabolic pathway can form a cycle if the product reacts to re-form the original substrate. Glucose and oxygen are required for cellular respiration. The products of these reactions include $CO_2$, water, and energy:

$$C_6H_{12}O_6 + O_2 \longrightarrow 6CO_2 + 6H_2O + \text{energy}$$

### *Glycolysis*

Cellular respiration begins with **glycolysis**, literally "the breaking of glucose" (fig. 4.9). Glycolysis occurs in the cytosol (the liquid portion of the cytoplasm), and because it does not directly require oxygen, it is also called the **anaerobic** (an″a-er-o′bik) phase of cellular respiration.

### *Aerobic Respiration*

The fate of pyruvic acid depends on oxygen availability. If oxygen is not present, then pyruvic acid enters an anaerobic pathway that yields lactic acid and limited energy (see fig. 8.10). If oxygen is present in sufficient quantity, the pyruvic acid generated by glycolysis can enter the more energy-efficient pathways of **aerobic respiration** (a″er-o′bik res″pĭ-ra′shun) in the mitochondria. The enzymes responsible for aerobic respiration reside on the cristae of the inner membranes of mitochondria, in the sequence in which they function.

In a mitochondrion, each molecule of pyruvic acid loses a carbon atom and binds a coenzyme to form a molecule of acetyl CoA, which can then combine with a 4-carbon compound to enter the **citric acid cycle** and then the **electron transport chain**. The final acceptor of electrons passed along the electron transport chain is oxygen. This is why the pathway is called "aerobic." (Because the reactions of the electron transport chain add phosphates to form ATP, they are also known as oxidative phosphorylation.) The aerobic reactions yield up to 36 ATP molecules per glucose (fig. 4.9).

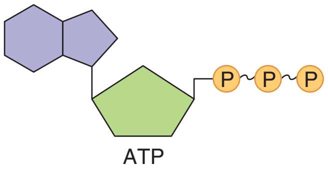


**FIGURE 4.6** Phosphate bonds contain the energy stored in ATP.

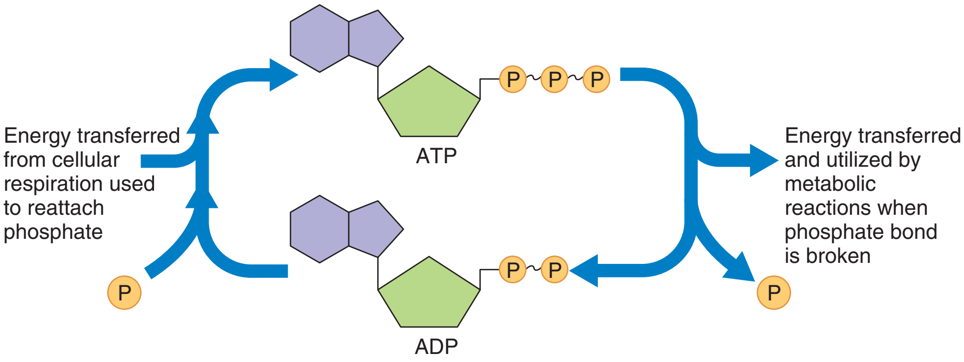

Energy transferred from cellular respiration used to reattach phosphate
P
P~P~P
ATP
Energy transferred and utilized by metabolic reactions when phosphate bond is broken
P~P
P
ADP

**FIGURE 4.7** ATP provides energy for metabolic reactions. Cellular respiration generates ATP.

**FIGURE 4.8** **A metabolic cycle.** A metabolic pathway forms a metabolic cycle when the product reacts and reforms the initial substrate.

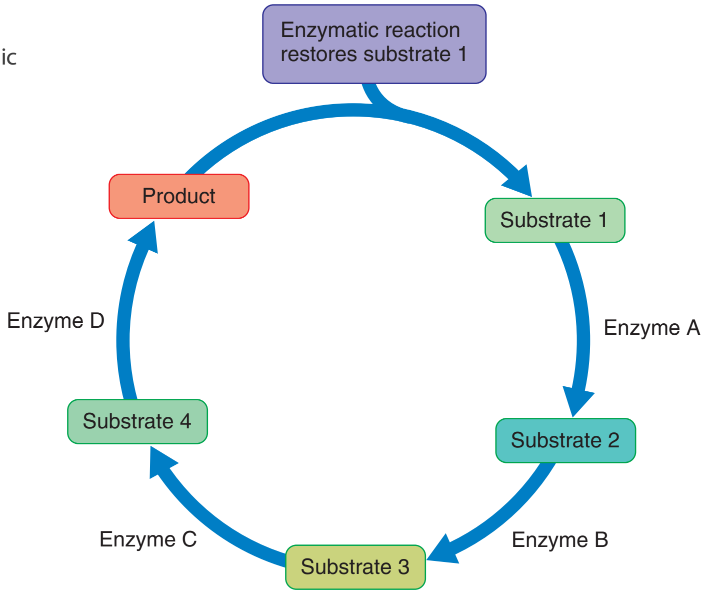

Enzymatic reaction restores substrate 1
Product
Substrate 1
Enzyme D
Enzyme A
Substrate 4
Substrate 2
Enzyme C
Enzyme B
Substrate 3

**FIGURE 4.9** AP|R Glycolysis takes place in the cytosol and does not require oxygen. Aerobic respiration takes place in the mitochondria, and only in the presence of oxygen. The products of glycolysis and aerobic respiration include ATP, heat, carbon dioxide, and water. Glycolysis generates 2 ATP, the citric acid cycle generates 2 ATP, and the electron transport chain releases 32 to 34 ATP molecules. Thus, the total yield of ATP molecules per glucose molecule is 36 to 38, depending on the cell type.

Q *Where in a cell does glycolysis occur?*

**Answer can be found in Appendix F on page 582.**

**Glycolysis**

① The 6-carbon sugar glucose is broken down in the cytosol into two 3-carbon pyruvic acid molecules with a net gain of 2 ATP and the release of high-energy electrons.

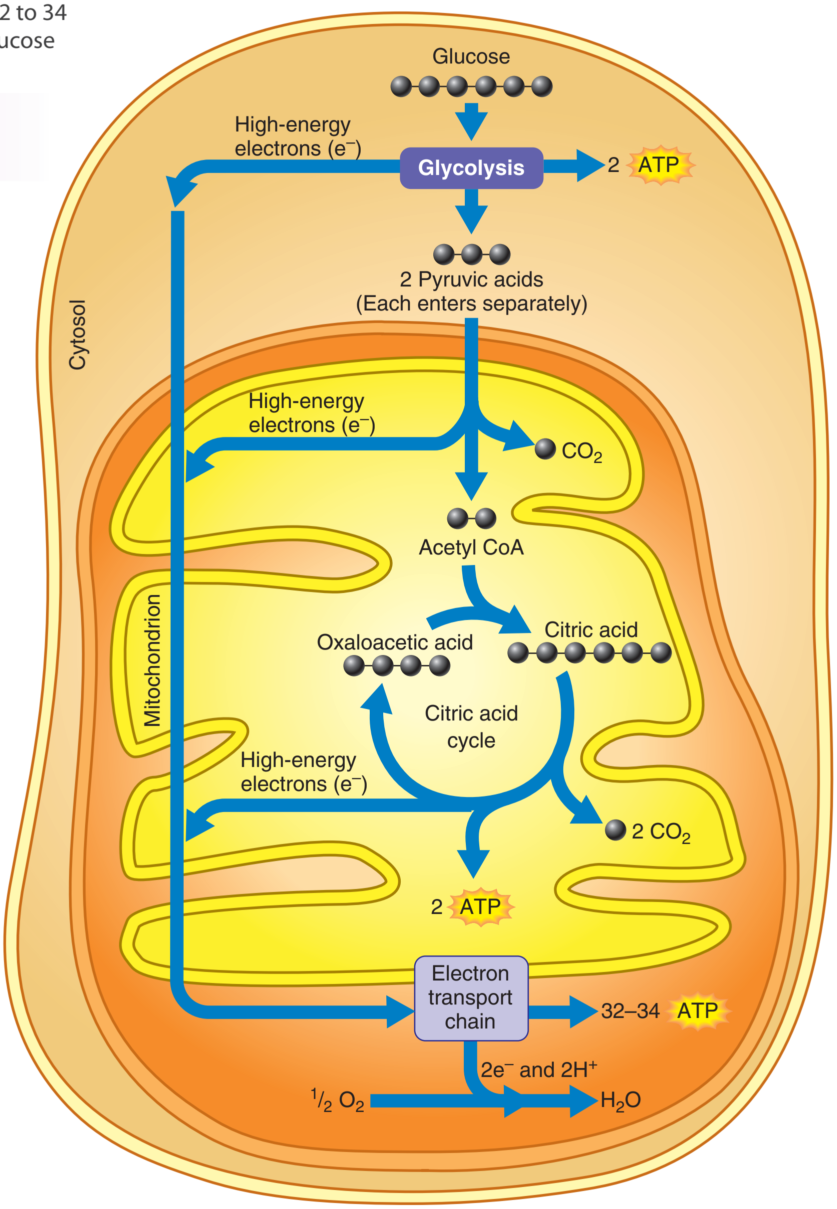
**Citric Acid Cycle**

② The 3-carbon pyruvic acids generated by glycolysis enter the mitochondria separately. Each loses a carbon (generating $CO_2$) and is combined with a coenzyme to form a 2-carbon acetyl coenzyme A (acetyl CoA). More high-energy electrons are released.

③ Each acetyl CoA combines with a 4-carbon oxaloacetic acid to form the 6-carbon citric acid, for which the cycle is named. For each citric acid, a series of reactions removes 2 carbons (generating 2 $CO_2$'s), synthesizes 1 ATP, and releases more high-energy electrons. The figure shows 2 ATP resulting directly from 2 turns of the cycle per glucose molecule that enters glycolysis.

**Electron Transport Chain**

④ The high-energy electrons still contain most of the chemical energy of the original glucose molecule. Special carrier molecules bring the high-energy electrons to a series of enzymes that transfer much of the remaining energy to more ATP molecules. The electrons eventually combine with hydrogen ions and an oxygen atom to form water. The function of oxygen as the final electron acceptor in this last step is why the overall process is called aerobic respiration.


Glucose
High-energy electrons $(e^-)$
Glycolysis
2 ATP
2 Pyruvic acids
(Each enters separately)
Cytosol
High-energy electrons $(e^-)$
$CO_2$
Acetyl CoA
Oxaloacetic acid
Citric acid
Mitochondrion
Citric acid cycle
High-energy electrons $(e^-)$
2 $CO_2$
2 ATP
Electron transport chain
32–34 ATP
$2e^-$ and $2H^+$
$^1/_2$ $O_2$
$H_2O$

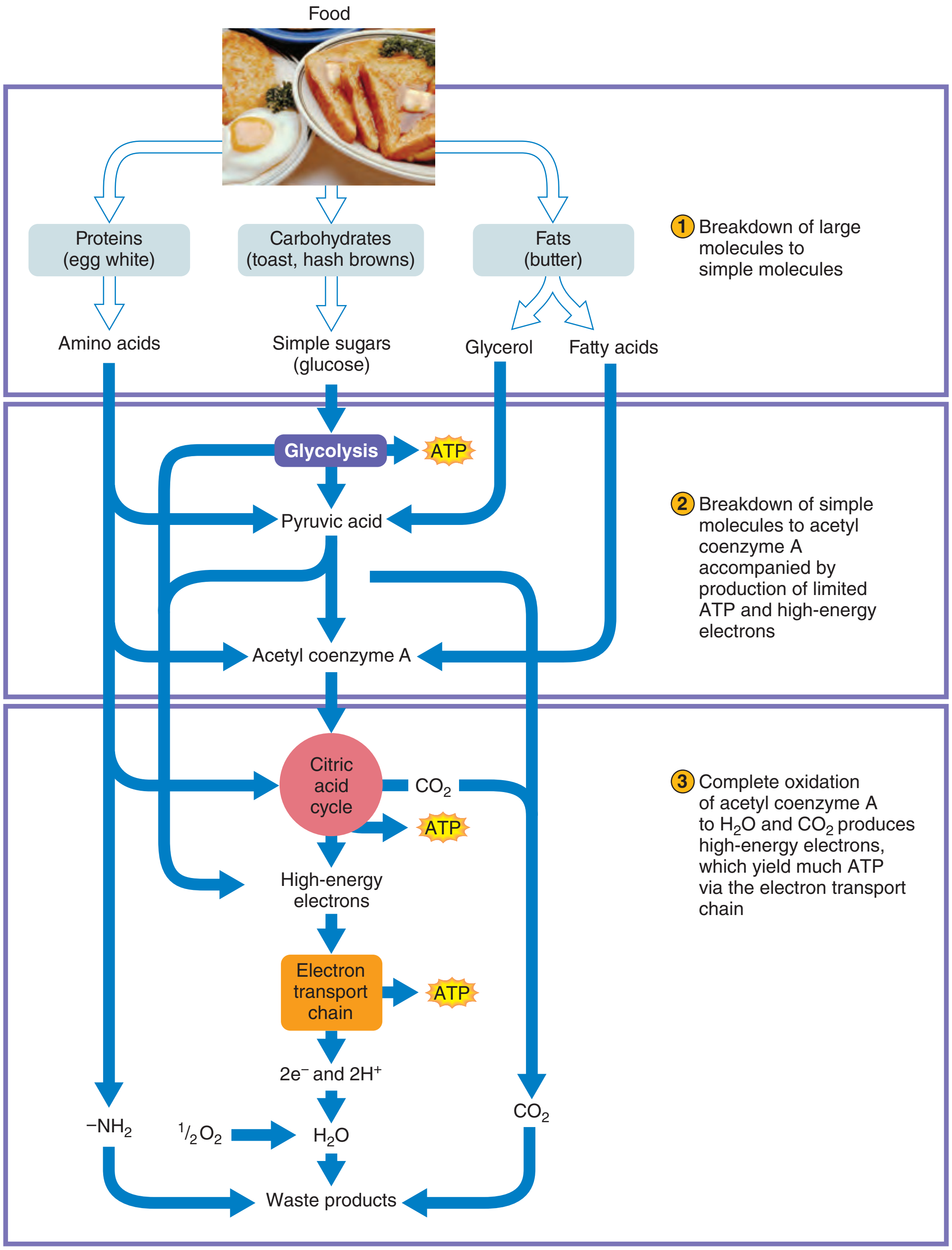

Food
Proteins (egg white)
Carbohydrates (toast, hash browns)
Fats (butter)
Amino acids
Simple sugars (glucose)
Glycerol
Fatty acids
① Breakdown of large molecules to simple molecules
Glycolysis
ATP
Pyruvic acid
Acetyl coenzyme A
② Breakdown of simple molecules to acetyl coenzyme A accompanied by production of limited ATP and high-energy electrons
Citric acid cycle
CO₂
ATP
High-energy electrons
Electron transport chain
ATP
2e⁻ and 2H⁺
–NH₂
½O₂
H₂O
CO₂
Waste products
③ Complete oxidation of acetyl coenzyme A to H₂O and CO₂ produces high-energy electrons, which yield much ATP via the electron transport chain

**FIGURE 4.10** A summary of the breakdown (catabolism) of proteins, carbohydrates, and fats.

For each glucose molecule that is completely broken down, up to 38 molecules of ATP are produced. Two of these ATP molecules come from glycolysis and the rest form during the aerobic phase. About half the energy released goes to ATP synthesis, while the rest ends up as heat. Complete oxidation of glucose also produces carbon dioxide and water. The carbon dioxide is eventually exhaled, and the water becomes part of the internal environment.

In humans, metabolism does not generate enough water to meet daily needs, so we must drink water to survive. In contrast, a small desert rodent, the kangaroo rat, can survive entirely on the water produced by aerobic respiration.

This section has dealt with the metabolism of glucose, a carbohydrate. The other macronutrients, so named because they are required in large amounts, are fats and proteins, and they are also broken down to release energy for ATP synthesis. For all three types of macronutrients, the final process is aerobic respiration, and the most common entry point is into the citric acid cycle as acetyl coenzyme A (acetyl CoA) (fig. 4.10). These metabolic pathways and their regulation are described further in chapter 15 (pp. 439–441).

## PRACTICE

14. Describe what happens during glycolysis.
15. What is the function of oxygen in cellular respiration?
16. What are the final products of cellular respiration?

## 4.5 | DNA (Deoxyribonucleic Acid)

Enzymes control essential metabolic reactions. Therefore, cells must have instructions for producing enzymes as well as other types of proteins. The sequences of building blocks of **DNA (deoxyribonucleic acid)** molecules hold the information to manufacture proteins in the form of a *genetic code.*

### Genetic Information

DNA molecules pass from parents to offspring when a sperm fertilizes an egg. As an offspring develops, mitosis passes the information in the DNA sequences of the chromosomes to new cells. A complete set of genetic instructions constitutes the **genome** (je′nōm). All cells except the sex cells contain two copies of the genome, one from each parent. Segments of the genome that encode proteins are called **genes** (jēnz). Only about 1.5% of the human genome encodes protein and it is called the **exome** (xōm). Much of the rest of the genome controls when and where genes become active to guide protein synthesis. Genetics Connection 4.1 describes how exome sequencing may aid diagnosis.

### DNA Molecules

Recall from chapter 2 (p. 55) that the building blocks of nucleic acids are nucleotides (see fig. 2.20, p. 55). They are joined so that the sugars and phosphates alternate, forming a long "backbone" to the polynucleotide chain (see fig. 2.21*b*, p. 56). DNA has two such polynucleotide chains.

In a DNA molecule, the nitrogenous bases project from the backbone and bind weakly to the bases of the other strand (fig. 4.11). The resulting structure is like a ladder in which the uprights represent the alternating sugar and phosphate backbones of the two strands, and the rungs represent the nitrogenous bases. In a nucleotide, the DNA base may be one of four types: *adenine* (A), *thymine* (T), *cytosine* (C), or *guanine* (G). A gene is a sequence of nucleotide bases along one DNA strand that specifies a particular protein's amino acid sequence.

The nitrogenous bases of DNA pair in specific ways: adenine only to thymine, and cytosine only to guanine. For example, a DNA strand with the base sequence A, C, G, C lies opposite and then binds to a strand with the sequence T, G, C, G (see the upper region of DNA in fig. 4.11). These pairs—A with T, and G with C—are called *complementary base pairs.* The long DNA molecule forms a double helix. It folds very tightly to fit inside a cell's nucleus. The two strands of a DNA double helix run in opposite orientations ("head-to-tail").

A molecule of DNA is typically millions of base pairs long. The great length of DNA molecules may seem quite a challenge to copy, or replicate, when a cell divides, but a set of special enzymes accurately and rapidly carries out this process.

**FACTS OF LIFE** If unwound, the DNA in a single cell would stretch to about the height of an average man. It obviously winds very tightly!

### DNA Replication

When a cell divides, each newly formed cell must have a copy of the original cell's genetic information (DNA) so it will be able to synthesize the proteins to build cellular parts and metabolize. This copying is called **replication** (rep″lĭ-ka′shun). It takes place during interphase of the cell cycle.

The double-stranded structure of DNA makes replication possible. As replication begins, hydrogen bonds between complementary base pairs in each DNA molecule break (fig. 4.12). The double helix unwinds and pulls apart, exposing the nitrogenous bases. Then an enzyme called DNA polymerase brings in new DNA nucleotides, and they form complementary pairs with the exposed bases. Other enzymes knit together the sugar-phosphate backbone. In this way, a new strand of complementary nucleotides forms along each of the old strands. This replication produces two complete DNA molecules, each with one old strand of the original molecule and one new strand. During mitosis, the two DNA molecules that form the two chromatids of each of the chromosomes separate so that one of these two DNA molecules passes to each of the new cells. Clinical Application 4.1 describes errors in DNA replication that change the sequence, generating a mutation.

## PRACTICE

17. Distinguish between *gene* and *genome.*
18. Why must DNA molecules replicate?
19. List the steps of DNA replication.

## GENETICS CONNECTION 4.1

## Exome Sequencing

The exome is the part of the genome that encodes protein. It is only 1.5% of the genome—45 million of the 3 billion DNA bases—but includes 85% of the mutations known to affect health.

Knowing the exome sequence of a patient with an unusual set of symptoms can help a physician make a diagnosis by revealing what is abnormal at the molecular level. Consider the following examples.

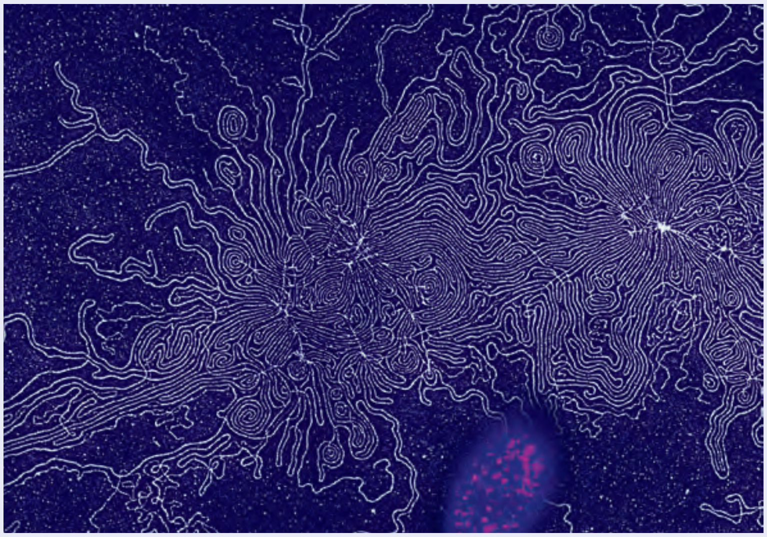


**FIGURE 4A** The exome is the part of the genome that encodes protein. The genes in the exome account for about 85% of inherited diseases.

### A Boy with Dissolving Intestines

By the time he was four years old, the boy had already had 100 surgeries, including removal of his colon. His gastrointestinal tract had been riddled with holes, starting at age two with an abscess in his rectum. Feces leaked from his intestines. He was fed by tube, and weighed less than 20 pounds. Doctors thought he was suffering from inflammatory bowel disease, but his symptoms seemed much too severe.

Researchers at the medical center where the boy was being treated had received funding to perform one of the very first exome-sequencing experiments, planned for 2014. When the boy's doctors implored the researchers to help, the date was moved up to 2009, and the boy became the first person to receive a diagnosis based on the results of exome sequencing.

The procedure uncovered more than 16,000 variations in gene sequences, and narrowed those down to 32 "candidate genes." The boy's symptoms were explained by a mutation in only one of those genes—a gene that normally prevents cells of the gastrointestinal tract from dying during infection. The disease corresponding to the mutation was known, but as an immune system disorder, not a digestive one. It was treatable with a cord-blood stem cell transplant, but until the exome sequencing, nobody knew that this condition was what the boy had. He received stem cells from an anonymous donor, rapidly gained weight, and today is much improved.

### In the Clinic

Each of the twelve children in a study conducted at a large medical center had developmental delay or intellectual disability, plus birth defects. None had a known inherited disease, or had been exposed to trauma or a toxin that might have caused the problems. Exome sequencing identified causative mutations for seven of the children. The information is practical. For example, one child's symptoms were due to a mutation in a gene that encodes a sodium channel protein, and the child would have reacted severely to certain drugs. The parents now know to avoid these drugs.

A larger study sequenced and analyzed hundreds of exomes from patients whom doctors had been unable to diagnose, and found answers for a fourth of them. The researchers had to narrow down 400 to 700 gene variants per patient! A two-year-old boy who had severe feeding difficulties and poor weight gain had a mutation known to cause Marfan syndrome, although his symptoms were atypical. One symptom of Marfan syndrome is an enlarged aorta, the largest artery. An ultrasound revealed that the boy indeed had a bulge in the wall of the aorta near the heart, which could have caused sudden death. He was successfully treated.

As the cost of exome sequencing falls, it may become a standard part of diagnostic medicine. Studies are under way to sequence exomes to better understand the physiology behind many diseases.

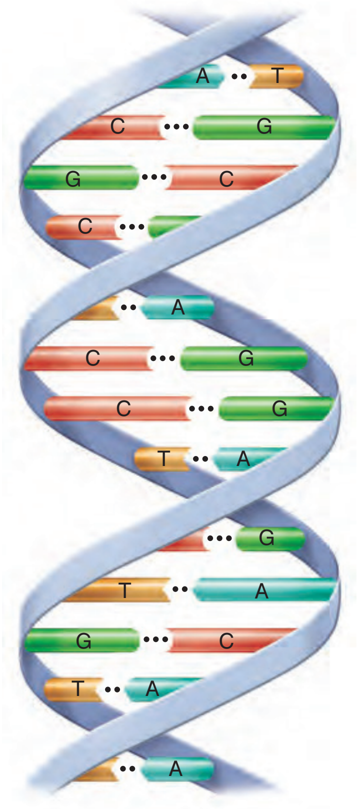


**FIGURE 4.11** DNA structure. The molecular "ladder" of a double-stranded DNA molecule twists into a double helix. The ladder's "rungs" consist of complementary base pairs held together by hydrogen bonds—A with T (or T with A) and G with C (or C with G).

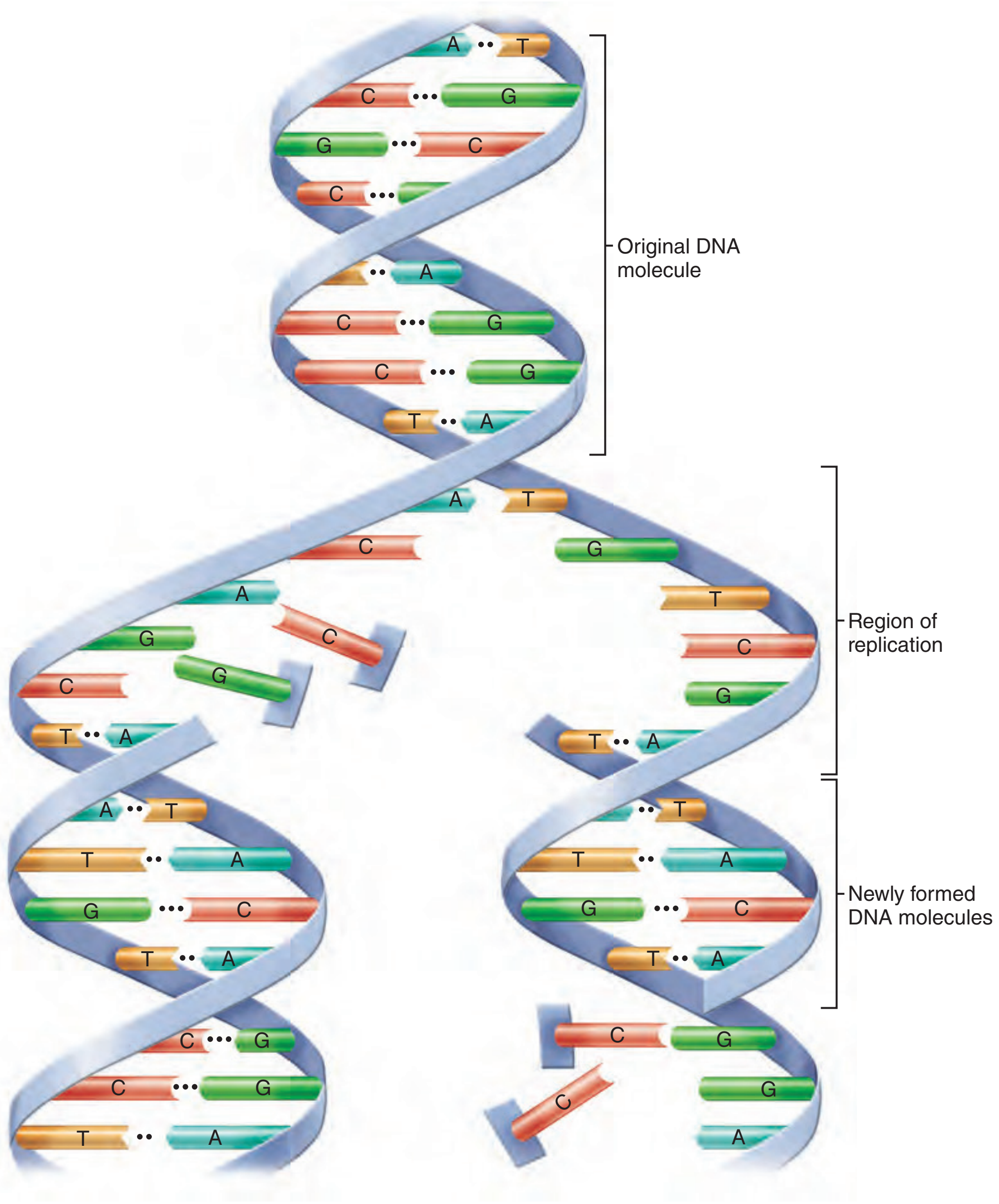


**FIGURE 4.12** DNA replication forms two double helices from one. When a DNA molecule replicates, its original strands separate locally. A new strand of complementary nucleotides forms along each original strand, using free nucleotides in the cell.

## 4.6 | Protein Synthesis

DNA provides the genetic instructions that a cell requires to synthesize proteins. Manufacturing proteins is a multistep, enzyme-catalyzed process.

### The Genetic Code—Instructions for Making Proteins

Cells can synthesize specific proteins because the sequence of nucleotide bases in the DNA of genes specifies a particular sequence of amino acid building blocks in a protein molecule. This correspondence of gene and protein building block sequence is called the **genetic code.**

Each of the twenty types of amino acids in a biological protein is represented in a DNA molecule by a particular sequence of three nucleotides. The DNA sequence G, G, T represents one type of amino acid; G, C, A represents another; and T, T, A a different one. Other nucleotide sequences encode the instructions for beginning or ending the synthesis of a protein molecule. Thus, the sequence of nucleotides in a DNA molecule denotes the order of amino acids in a protein molecule, as well as where to start or stop that protein's synthesis.

## CLINICAL APPLICATION 4.1

### Mutations

Like typing a long text message, replicating DNA is an error-prone process. A newly replicated gene may have a change in the sequence from what is dictated in the original, complementary strand. This error is a type of mutation.

Fortunately, cells can scan newly replicated DNA, detect mutations, and correct some of them, like a cell phone keypad's autocorrect feature. When DNA repair fails, health may suffer. People with faulty DNA repair tend to develop cancers, because cells cannot correct cancer-causing mutations.

Mutations are inherited in two ways. A recessive mutation must be present in both copies of the affected gene to cause symptoms. Each of us has a single copy of 400 to 800 such mutations that could harm health. A dominant mutation exerts an effect even if present in only one gene copy. Databases organize human mutations into categories, such as by affected body part, mutations common in a particular nation or population group, and all known mutations that cause a disease.

Tests for many single-gene diseases have been available for decades, and they are important in diagnosis and selecting appropriate treatments. Because most mutations are present from conception, some genetic tests may detect conditions before symptoms arise.

**TABLE 4.1 A Comparison of DNA and RNA Molecules**

| | DNA | RNA |
|---|---|---|
| Main location | Part of chromosomes, in nucleus | Cytoplasm |
| 5-carbon sugar | Deoxyribose | Ribose |
| Basic molecular structure | Double-stranded | Single-stranded |
| Nitrogenous bases included | Adenine, thymine, cytosine, guanine | Adenine, uracil, cytosine, guanine |
| Major functions | Contains genetic code for protein synthesis; replicates prior to cell division | mRNA carries transcribed DNA information to cytoplasm and acts as template for synthesis of protein molecules; tRNA carries amino acids to mRNA |

### *Transcription*

DNA molecules stay in a cell's nucleus, maintaining the genetic information, but protein synthesis occurs in the cytoplasm. The genetic information reaches the cytoplasm by being copied into molecules of RNA (ribonucleic acid), which can exit the nucleus because they are much shorter than the DNA that composes chromosomes and they are single-stranded. The process of synthesizing RNA is called **transcription. Messenger RNA (mRNA)** is the type of RNA that carries a gene's message out of the nucleus. Other types of RNA also help to build proteins.

RNA (ribonucleic acid) molecules differ from DNA molecules in several ways (table 4.1). RNA molecules are single-stranded, and their nucleotides include the sugar ribose rather than deoxyribose. Like DNA, each RNA nucleotide includes one of four nitrogenous bases. However, whereas adenine, cytosine, and guanine nucleotides are in both DNA and RNA, thymine nucleotides are only in DNA. In place of thymine nucleotides, RNA molecules have *uracil* (U) nucleotides.

The enzyme RNA polymerase synthesizes mRNA following the rules of complementary base pairing. For example, the DNA sequence A, T, G, C, G specifies the complementary mRNA bases U, A, C, G, C (table 4.2). Specific DNA sequences outside genes signal which of the two DNA strands contains the information to build a protein. RNA polymerase also recognizes sequences in the DNA that indicate where the gene begins, where it stops, and the correct direction to read the DNA, just

**TABLE 4.2 Complementary Base Pairs**

| Complementary strands of a DNA molecule | | Transcribed strand of DNA | Complementary strand of mRNA |
|---|---|---|---|
| A | T | A | U |
| T | A | T | A |
| C | G | C | G |
| G | C | G | C |

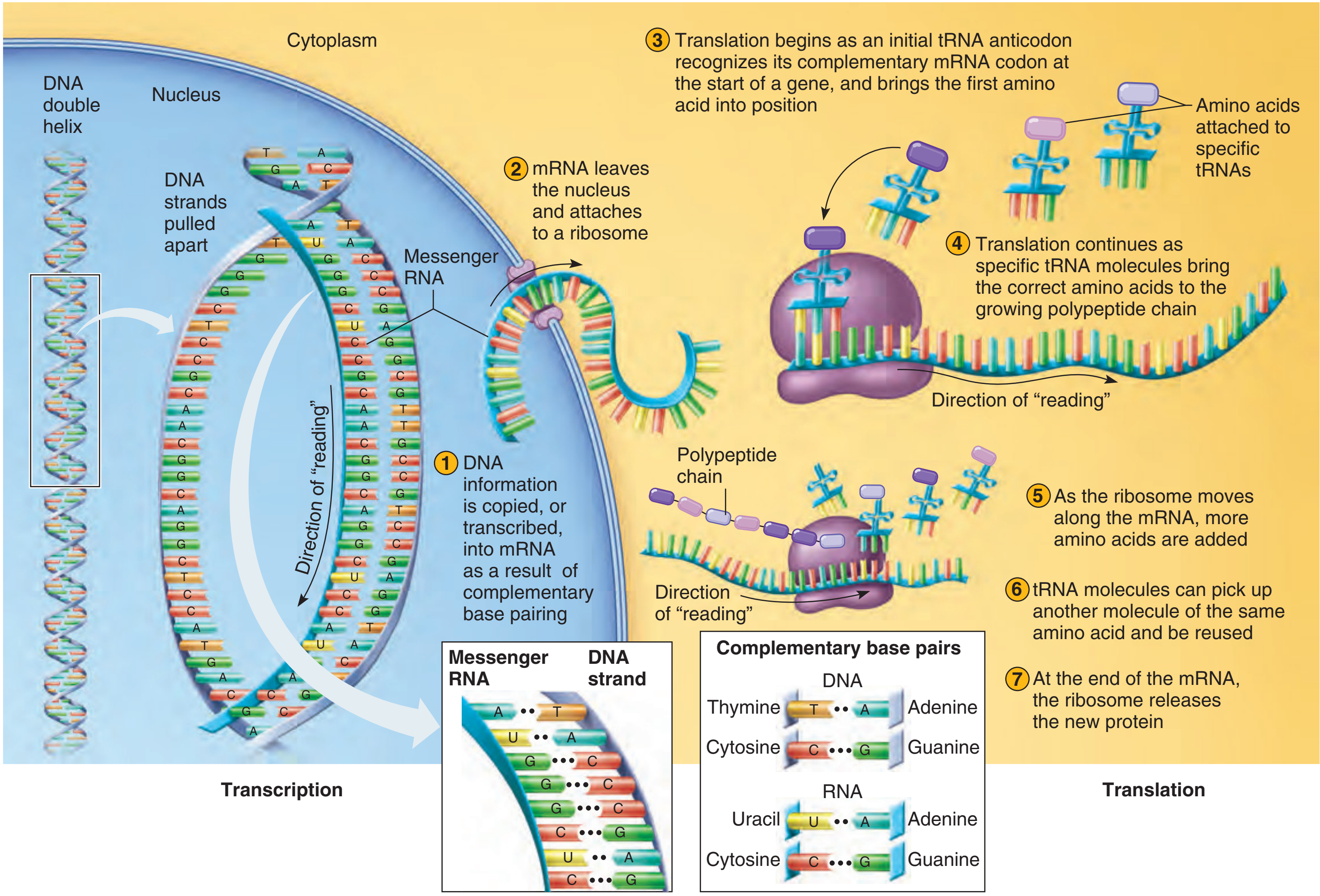
like a sentence. When the RNA polymerase reaches the end of the gene, it releases the newly formed mRNA. Transcription is complete.

Many genes are transcribed in "pieces" called exons. Sections called introns are spliced out of the mRNA before a protein is synthesized. Cells can transcribe and assemble different combinations of exons from a particular gene, creating slightly different forms of a protein that can function in different cell types or under specific conditions.

### Translation

Each amino acid in a protein is specified by three contiguous bases in the DNA sequence. Those bases, in the correct order, are represented by a three-base sequence, called a **codon** (ko′don), in mRNA (table 4.3). In addition to the mRNA codons that specify amino acids, the sequence AUG represents the "start" of a gene, and three other mRNA base sequences indicate "stop." To guide protein synthesis, an mRNA molecule must leave the nucleus and associate with a ribosome in the cytoplasm. There the series of codons on mRNA is translated from the "language" of nucleic acids to the "language" of amino acids. This process of protein synthesis is appropriately called **translation.**

Building a protein molecule requires ample supplies of the correct amino acids in the cytoplasm and positioning them in the order specified along a strand of mRNA. A second kind of RNA molecule called **transfer RNA (tRNA)** correctly aligns amino acids, which are then linked by enzymatic action to form proteins (fig. 4.13). Like mRNA, tRNA is synthesized in the


Cytoplasm
DNA double helix
Nucleus
DNA strands pulled apart
Messenger RNA
Direction of "reading"
Amino acids attached to specific tRNAs
Direction of "reading"
Polypeptide chain
Direction of "reading"
Transcription
Translation
Messenger RNA
DNA strand
A •• T
U •• A
G ••• C
G ••• C
G ••• C
C ••• G
U •• A
C ••• G
Complementary base pairs
DNA
Thymine T •• A Adenine
Cytosine C ••• G Guanine
RNA
Uracil U •• A Adenine
Cytosine C ••• G Guanine

① DNA information is copied, or transcribed, into mRNA as a result of complementary base pairing

② mRNA leaves the nucleus and attaches to a ribosome

③ Translation begins as an initial tRNA anticodon recognizes its complementary mRNA codon at the start of a gene, and brings the first amino acid into position

④ Translation continues as specific tRNA molecules bring the correct amino acids to the growing polypeptide chain

⑤ As the ribosome moves along the mRNA, more amino acids are added

⑥ tRNA molecules can pick up another molecule of the same amino acid and be reused

⑦ At the end of the mRNA, the ribosome releases the new protein

**FIGURE 4.13** APR Protein synthesis. DNA information is transcribed into mRNA, which in turn is translated into a sequence of amino acids. The inset shows complementary base pairs in DNA and RNA.

Q *What is the name of the molecule that carries DNA information so that it can be translated into protein?*

**Answer can be found in Appendix F on page 582.**

**TABLE 4.3** Codons (mRNA Three-Base Sequences)

| | SECOND LETTER | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| FIRST LETTER | U | | C | | A | | G | | THIRD LETTER |
| U | UUU | phenylalanine (phe) | UCU | serine (ser) | UAU | tyrosine (tyr) | UGU | cysteine (cys) | U |
| | UUC | | UCC | | UAC | | UGC | | C |
| | UUA | leucine (leu) | UCA | | UAA | STOP | UGA | STOP | A |
| | UUG | | UCG | | UAG | STOP | UGG | tryptophan (trp) | G |
| C | CUU | leucine (leu) | CCU | proline (pro) | CAU | histidine (his) | CGU | arginine (arg) | U |
| | CUC | | CCC | | CAC | | CGC | | C |
| | CUA | | CCA | | CAA | glutamine (gln) | CGA | | A |
| | CUG | | CCG | | CAG | | CGG | | G |
| A | AUU | isoleucine (ile) | ACU | threonine (thr) | AAU | asparagine (asn) | AGU | serine (ser) | U |
| | AUC | | ACC | | AAC | | AGC | | C |
| | AUA | | ACA | | AAA | lysine (lys) | AGA | arginine (arg) | A |
| | AUG | START methionine (met) | ACG | | AAG | | AGG | | G |
| G | GUU | valine (val) | GCU | alanine (ala) | GAU | aspartic acid (asp) | GGU | glycine (gly) | U |
| | GUC | | GCC | | GAC | | GGC | | C |
| | GUA | | GCA | | GAA | glutamic acid (glu) | GGA | | A |
| | GUG | | GCG | | GAG | | GGG | | G |

nucleus and sent into the cytoplasm, where it assists in constructing a protein molecule.

Because twenty different types of amino acids form biological proteins, at least twenty different types of tRNA molecules must be available, one for each type of amino acid. Each type of tRNA has a region at one end that consists of three nucleotides that form complementary base pairs with a specific mRNA codon. The three nucleotides in the tRNA are called an **anticodon** (an″tĭ-ko′don). In this way, tRNA carries its amino acid to a correct position on an mRNA strand. This action occurs on a ribosome (fig. 4.13).

There are 64 possible types of tRNA anticodons, because there are this many possible triplets. Some amino acids may bind to more than one type of tRNA.

As protein synthesis begins, a ribosome binds an mRNA molecule. A tRNA molecule with the complementary anticodon holding its amino acid forms hydrogen bonds with the first mRNA codon. A second tRNA then binds the next codon, bringing its amino acid to an adjacent site on the ribosome. Then a peptide bond forms between the two amino acids, beginning a chain. The first tRNA molecule is released from its amino acid and is recycled to the cytoplasm (fig. 4.14). This process repeats as the ribosome moves along the mRNA molecule. The amino acids delivered by the tRNA molecules are added one at a time to the developing protein.

As the protein molecule forms, it folds into its unique conformation and is then released to become a separate functional molecule. Correct protein folding is essential to health. In cells, misfolded proteins are threaded through spool-shaped structures called *proteasomes*. Here, they are either refolded into the functional conformation, or destroyed if they are too abnormal.

A gene that is transcribed and translated into a protein is said to be *expressed*. The types and amounts of proteins in a cell, which can change with changing conditions, largely determine the function a cell performs in the body. Gene expression is the basis for cell differentiation, described in chapter 3 (p. 82).

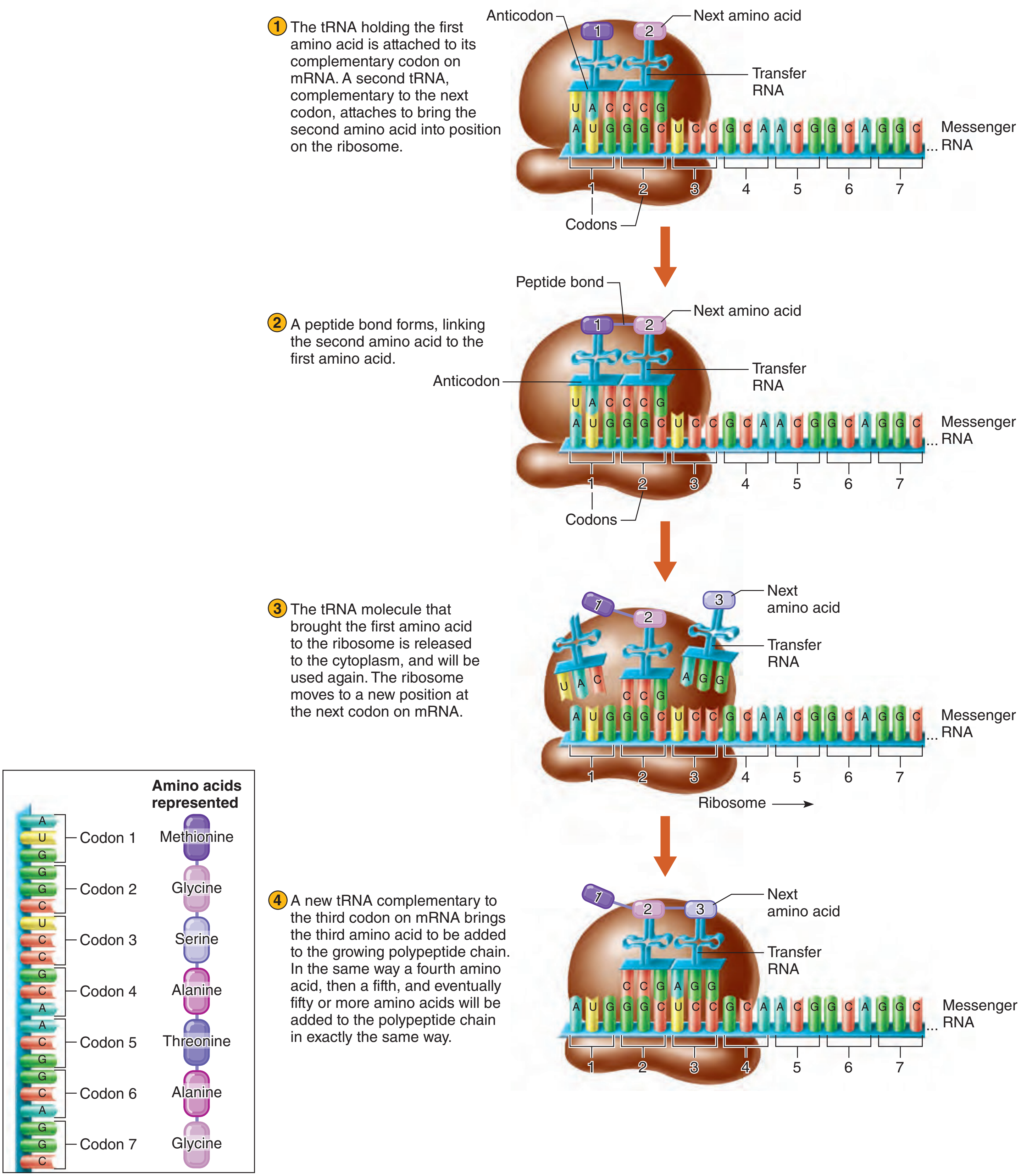
## PRACTICE

20 Define *genetic code*.

21. What is the function of DNA?

22. How is genetic information carried from the nucleus to the cytoplasm?

23. List the steps of protein synthesis.



① The tRNA holding the first amino acid is attached to its complementary codon on mRNA. A second tRNA, complementary to the next codon, attaches to bring the second amino acid into position on the ribosome.

② A peptide bond forms, linking the second amino acid to the first amino acid.

③ The tRNA molecule that brought the first amino acid to the ribosome is released to the cytoplasm, and will be used again. The ribosome moves to a new position at the next codon on mRNA.

④ A new tRNA complementary to the third codon on mRNA brings the third amino acid to be added to the growing polypeptide chain. In the same way a fourth amino acid, then a fifth, and eventually fifty or more amino acids will be added to the polypeptide chain in exactly the same way.

Anticodon
Next amino acid
Transfer RNA
U A C C C G
A U G G G C U C C G C A A C G G C A G G C
Messenger RNA
1 2 3 4 5 6 7
Codons
Peptide bond
Next amino acid
Anticodon
Transfer RNA
Messenger RNA
Codons
Next amino acid
Transfer RNA
U A C
C C G
A G G
Messenger RNA
Ribosome
Next amino acid
Transfer RNA
C C G A G G
Messenger RNA
Amino acids represented
Codon 1 Methionine
Codon 2 Glycine
Codon 3 Serine
Codon 4 Alanine
Codon 5 Threonine
Codon 6 Alanine
Codon 7 Glycine

**FIGURE 4.14** APR Protein synthesis occurs on ribosomes. Molecules of transfer RNA (tRNA) attach to and carry specific amino acids, aligning them in the sequence determined by the codons of mRNA. These amino acids, connected by peptide bonds, form a polypeptide chain of a protein molecule. The inset shows the correspondence between mRNA codons and the specific amino acids they encode.

## Summary Outline

### 4.1 Introduction (p. 87)

*A cell continuously carries on thousands of metabolic reactions that maintain life and enable specialization. Cellular metabolism acquires, stores, and releases energy.*

### 4.2 Metabolic Reactions (p. 87)

1. Anabolism
   a. Anabolism builds large molecules from smaller molecules.
   b. In dehydration synthesis, water forms, and smaller molecules join by sharing atoms.
   c. Carbohydrates are synthesized from monosaccharides, fats from glycerol and fatty acids, proteins from amino acids, and nucleotides from nucleic acids.
2. Catabolism
   a. Catabolism breaks down larger molecules into smaller ones.
   b. In hydrolysis, a water molecule is split as an enzyme breaks the bond between two parts of a molecule.
   c. Hydrolysis breaks down carbohydrates into monosaccharides, fats into glycerol and fatty acids, proteins into amino acids, and nucleic acids into nucleotides.

### 4.3 Control of Metabolic Reactions (p. 88)

*Enzymes control metabolic reactions, which include many specific chemical changes.*

1. Enzyme action
   a. Enzymes lower the amount of energy required to start chemical reactions.
   b. Enzymes are molecules that promote metabolic reactions without being consumed (catalysis).
   c. An enzyme acts upon a specific substrate molecule.
   d. The shape of an enzyme molecule fits the shape of its substrate.
   e. When an enzyme combines with its substrate, the substrate changes, a product forms, and the enzyme is released in its original form.
   f. The rate of an enzyme-controlled reaction depends partly upon the numbers of enzyme and substrate molecules and the enzyme's efficiency.
2. Enzymes and metabolic pathways
   a. A sequence of enzyme-controlled reactions constitutes a metabolic pathway.
   b. Regulatory enzymes in limited numbers set rates of metabolic pathways.
   c. Regulatory enzymes become saturated when substrate concentrations exceed a certain level.
3. Factors that alter enzymes
   a. A cofactor is a nonprotein necessary for a specific enzyme to function. It may be a coenzyme, which is organic and can be a vitamin.
   b. Most enzymes are proteins. Harsh conditions undo, or denature, their specific shapes.
   c. Heat, radiation, electricity, certain chemicals, and extreme pH values denature enzymes.

### 4.4 Energy for Metabolic Reactions (p. 90)

*Energy is the capacity to do work. Common forms of energy include heat, light, sound, electrical energy, mechanical energy, and chemical energy.*

1. Release of chemical energy
   a. Most metabolic processes use chemical energy released when chemical bonds break.
   b. The energy released from glucose breakdown during cellular respiration drives the reactions of cellular metabolism.
2. ATP Molecules
   a. Energy is captured in the bond of the terminal phosphate of each ATP.
   b. When a cell requires energy, the terminal phosphate bond of an ATP molecule breaks, releasing stored energy.
   c. An ATP molecule that loses its terminal phosphate becomes ADP.
   d. An ADP molecule that captures energy and a phosphate becomes ATP.
3. Cellular Respiration
   a. Glycolysis
      (1) The first phase of glucose decomposition does not directly require oxygen (anaerobic).
      (2) Some of the energy released is transferred to ATP.
   b. Aerobic respiration
      (1) The second phase of glucose decomposition requires oxygen.
      (2) Many more ATP molecules form during this phase than during the anaerobic phase.
      (3) The final products of glucose breakdown are carbon dioxide, water, and energy (ATP and heat).

### 4.5 DNA (Deoxyribonucleic Acid) (p. 94)

*DNA molecules contain information that instructs a cell how to synthesize enzymes and other proteins.*

1. Genetic information
   a. Inherited traits result from DNA information passed from parents to offspring.
   b. A complete set of genetic instructions is a genome.
   c. A gene is a DNA sequence that contains the information for making a particular protein.
2. DNA molecules
   a. A DNA molecule consists of two strands of nucleotides wound into a double helix.
   b. The nucleotides of a DNA strand are linked in a specific sequence.
   c. The nucleotides of each strand pair with those of the other strand in a complementary fashion (A with T and G with C).
3. DNA replication
   a. When a cell divides, each new cell requires a copy of the older cell's genetic information.
   b. DNA molecules replicate during interphase of the cell cycle.
   c. Each new DNA molecule has one old strand and one new strand.

### 4.6 Protein Synthesis (p. 96)

*Genes provide instructions for making proteins, which take part in many aspects of cell function.*

1. The genetic code—instructions for making proteins
   a. A sequence of DNA nucleotides encodes a sequence of amino acids.
   b. RNA molecules transfer genetic information from the nucleus to the cytoplasm.
   c. Transcription
      (1) Most RNA molecules are single-stranded; they contain ribose instead of deoxyribose and uracil nucleotides in place of thymine nucleotides.

(2) Messenger RNA (mRNA) molecules consist of nucleotide sequences that are complementary to those of exposed strands of DNA.

(3) Messenger RNA molecules associate with ribosomes and provide patterns for the synthesis of protein molecules.

d. Translation

(1) A ribosome binds to an mRNA molecule.

(2) Molecules of tRNA position amino acids along a strand of mRNA.

(3) Amino acids released from the tRNA molecules join and form a protein molecule that folds into a unique shape.

## CHAPTER ASSESSMENTS

### 4.1 Introduction

**1.** Explain the function of cellular metabolism. (p. 87)

**2.** Explain why enzymes are important in the body. (p. 87)

### 4.2 Metabolic Reactions

**3.** Distinguish between anabolism and catabolism. (p. 87)

**4.** Distinguish between dehydration synthesis and hydrolysis. (pp. 87–88)

### 4.3 Control of Metabolic Reactions

**5.** Describe how an enzyme interacts with its substrate. (p. 89)

**6.** Define *active site.* (p. 89)

**7.** Define *metabolic pathway.* (p. 89)

**8.** Explain how one enzyme can control the rate of a metabolic pathway. (p. 90)

**9.** Define *cofactor.* (p. 90)

**10.** Exposure to radiation can ___________ an enzyme and change its shape to the point where it becomes inactive. (p. 90)

a. catalyze
b. decompose
c. synthesize
d. denature

### 4.4 Energy for Metabolic Reactions

**11.** Explain how oxidation of molecules inside cells differs from burning materials outside of cells. (p. 91)

**12.** Explain the importance of ATP, and the relationship of ATP to ADP. (p. 91)

**13.** Distinguish between anaerobic and aerobic phases of cellular respiration. (p. 91)

**14.** Match the parts of cellular respiration to their associated activities. (p. 91)

(1) electron transport chain
(2) glycolysis
(3) citric acid cycle

A. glucose molecules are broken down into pyruvic acid
B. the final electron acceptor is oxygen
C. acetyl CoA molecules are broken down to release $CO_2$ and high-energy electrons

**15.** Identify the final acceptor of the electrons released in the reactions of cellular respiration. (p. 91)

**16.** Identify the cellular respiration pathway where glucose, fats, and proteins commonly enter. (p. 93)

### 4.5 DNA (Deoxyribonucleic Acid)

**17.** Distinguish between a gene and a genome. (p. 94)

**18.** DNA information provides instructions for the cell to ____. (p. 94)

a. manufacture carbohydrate molecules
b. synthesize lipids
c. manufacture RNA from amino acids
d. synthesize protein molecules

**19.** Explain why DNA replication is essential. (p. 94)

**20.** Describe the events of DNA replication. (p. 94)

### 4.6 Protein Synthesis

**21.** Calculate the number of amino acids encoded by a DNA sequence of 27 nucleotides. (p. 96)

**22.** If a strand of DNA has the sequence A T G C G A T C C G C, then the sequence of an mRNA molecule transcribed from it is ___________. (p. 97)

**23.** Distinguish between transcription and translation. (pp. 97–98)

**24.** Describe the function of a ribosome in protein synthesis. (p. 99)

**25.** Define *gene expression.* (p. 99)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 2.2, 4.4, 4.6

**1.** The chapter discusses several specific types of chemical bonds. Describe each of the following, and explain why each is important.

a. High-energy phosphate bond
b. Peptide bond
c. The bond between an mRNA codon and a tRNA anticodon

### OUTCOMES 4.2, 4.3

**2.** How can the same biochemical be both a reactant (a starting material) and a product?

### OUTCOMES 4.3, 4.4

**3.** What effect might changes in the pH of body fluids or body temperature that accompany illness have on enzymes?

### OUTCOME 4.3, 4.5

**4.** Explain how proteins assist in DNA replication.

### OUTCOME 4.4

**5.** After finishing a grueling marathon, a runner exclaims, “Whew, I think I’ve used up all my ATP!” Could this be possible?

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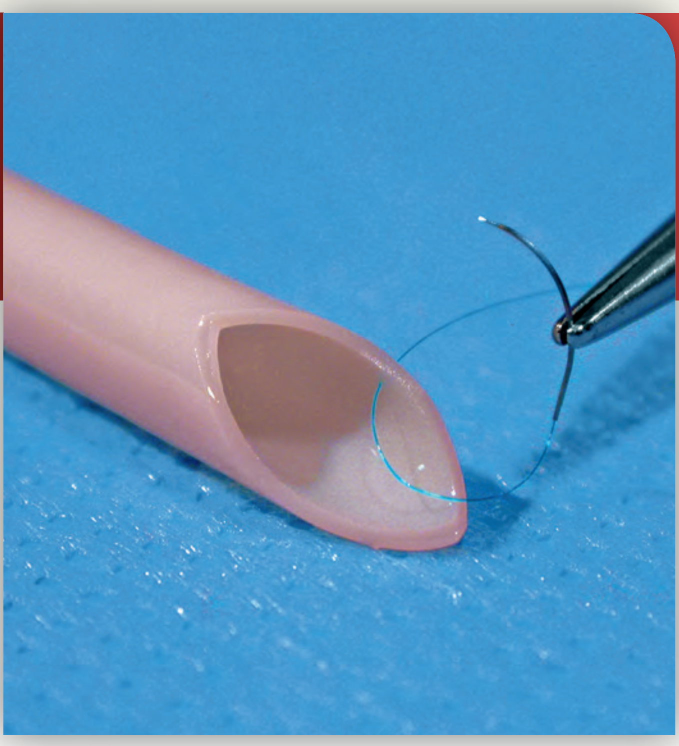
# 5

# Tissues



*This replacement "blood vessel" is the product of tissue engineering.*

Tissue engineering. If an appliance part is damaged or fails, replacing it is simple. Not so for the human body. Donor organs and tissues for transplant are in short supply, so in the future spare parts may come from tissue engineering. In this technology, a patient's cells, extracellular matrix, and other biochemicals are grown with a synthetic scaffold to form an implant. The cells come from the patient, so the immune system does not reject them. Tissue engineering has provided skin, cartilage, bone, and blood vessels. Combining engineered tissues into structures that can replace organs is where the creativity comes in. Consider the replacement bladder.

Each year in the United States, about 10,000 people need their urinary bladders repaired or replaced. Typically a urologic surgeon replaces part of the urinary bladder with the large intestine. However, the function of the intestine is to absorb, and the function of the bladder is to hold waste. Tissue engineering is providing a better replacement bladder. The natural organ is balloonlike, with layers of smooth muscle, connective tissue, and a lining of urothelium.

Researchers pioneered replacement bladders in children who have birth defects in which the malfunctioning bladder can harm the kidneys. Each patient donated a postage-stamp-size sample of bladder tissue that consisted of about a million cells, from which the researchers separated progenitor cells—for smooth muscle and urothelium—and let them divide in culture in a specific mixture of growth factors. Within seven weeks the million cells had divided to yield 1.5 billion cells, which were seeded onto domes made of synthetic material. The confluent layers of cells that formed were attached to the lower portions of the patients' bladders, after removing the upper portions. The scaffolds degenerated over time, leaving new bladders built from the patients' own cells. Today tissue-engineered bladders are also used in adults whose bladders have been removed to treat cancer.

## LEARNING OUTCOMES

***After studying this chapter, you should be able to do the following:***

### 5.1 Introduction

1. List the four major tissue types, and indicate a function of each type. (p. 105)

### 5.2 Epithelial Tissues

2. Describe the general characteristics and functions of epithelial tissue. (p. 105)
3. Name the types of epithelium and identify an organ in which each is found. (pp. 106–109)
4. Explain how glands are classified. (pp. 109–111)

### 5.3 Connective Tissues

5. Compare and contrast the ground substance, cells, and fibers in different types of connective tissue. (pp. 113–115)
6. Describe the major functions of each type of connective tissue. (pp. 116–119)
7. Identify a location where each type of connective tissue is found. (pp. 116–119)

### 5.4 Types of Membranes

8. Distinguish among the four major types of membranes. (p. 119)

### 5.5 Muscle Tissues

9. Distinguish among the three types of muscle tissues. (p. 121)

### 5.6 Nervous Tissues

10. Describe the general characteristics and functions of nervous tissue. (p. 122)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**adip-** [fat] *adip*ose tissue: Tissue that stores fat.

**chondr-** [cartilage] *chondr*ocyte: Cartilage cell.

**-cyt** [cell] osteo*cyt*e: Bone cell.

**epi-** [upon] *epi*thelial tissue: Tissue that covers all free body surfaces.

**-glia** [glue] neuro*glia*: Cells that support neurons; part of nervous tissue.

**inter-** [between] *inter*calated disc: Band between adjacent cardiac muscle cells.

**macr-** [large] *macr*ophage: Large phagocytic cell.

**os-** [bone] *os*seous tissue: Bone tissue.

**pseud-** [false] *pseud*ostratified epithelium: Tissue with cells that appear to be in layers, but are not.

**squam-** [scale] *squam*ous epithelium: Tissue with flattened or scalelike cells.

**strat-** [layer] *strat*ified epithelium: Tissue with cells in layers.

---

## 5.1 | Introduction

Cells, the basic units of structure and function in the human organism, are organized into groups called **tissues** (tish′uz). Each type of tissue is composed of similar cells with a common function.

The tissues of the human body are of four major types: *epithelial, connective, muscle,* and *nervous.* Epithelial tissues form protective coverings and function in secretion and absorption. Connective tissues support soft body parts and bind structures together. Muscle tissues produce body movements, and nervous tissues conduct impulses that help control and coordinate body activities. Table 5.1 compares the four major tissue types.

Keep in mind that tissues are three-dimensional structures. Micrographs are photos of extremely thin slices (sections) of prepared tissue specimens, and may show more than one tissue type. The advantage of observing thin slices is that light passes through them more readily, making structures easier to see and photograph under magnification; but the relationship of the structures in three dimensions may not be obvious. Figure 5.1 shows how a tubular structure would appear (a) in a cross section and (b) in a longitudinal section (see also fig. 1.12, page 20).

Throughout this chapter, three-dimensional line drawings (for example, fig. 5.2*a*) are included with the micrograph (for example, fig. 5.2*b,c*) to emphasize the orientation and distinguishing characteristics of the specific tissues, as well as locator icons (for example, the fig. 5.2 locator icon indicates where in the body that particular tissue might be found).

### PRACTICE

1. What is a tissue?
2. List the four major types of tissues.

## 5.2 | Epithelial Tissues

### General Characteristics

**Epithelial** (ep″ĭ-the′le-al) **tissues** are found throughout the body. Epithelium covers organs, forms the inner lining of body cavities, and lines hollow organs. It always has a *free (apical) surface* exposed to the outside or internally to an open space. The underside of this tissue is anchored to connective tissue by a thin, nonliving layer called the **basement membrane.**

As a rule, epithelial tissues lack blood vessels. However, nutrients diffuse to epithelium from underlying connective tissues, which have abundant blood vessels.

Epithelial cells readily divide. As a result, injuries heal rapidly as new cells replace lost or damaged ones. For example, skin cells and cells that line the stomach and intestines are continually damaged and replaced.

### CAREER CORNER
### Medical Transcriptionist

The busy pediatrician reads her young patient's recent medical history on her hand-held device just minutes before the appointment, and learns that after an anxious few moments when the fetal heart rate dipped, the birth had gone well. The clear writing of the medical transcriptionist informed the physician.

A medical transcriptionist combines excellent language and keyboarding skills with knowledge of the terminology of pathology, anatomy, and physiology, including many acronyms and abbreviations. In addition to excellence in spelling, grammar, and editing, a medical transcriptionist may also correct and edit documents generated from voice-recognition software.

Medical transcriptionists work in physicians' offices, in hospitals and clinics, for insurance companies, and for hospice and home health-care organizations. Some medical transcriptionists work from home. Medical transcriptionists create and maintain physical exam reports, autopsy reports, test result interpretations, referral letters, medical history notes, discharge summaries, and descriptions of surgical procedures.

Most medical transcriptionists have a two-year associate's degree or have completed a one-year certificate program. It is an excellent career choice for those who are interested in health and have an ease with language.

Epithelial cells are tightly packed. Consequently, these cells form effective protective barriers in such structures as the outer layer of the skin and the lining of the mouth. Other epithelial functions include secretion, absorption, and excretion.

Epithelial tissues are classified according to cell shape and the number of cell layers. Epithelial tissues that are composed of thin, flattened cells are *squamous;* those with cube-shaped cells are *cuboidal;* and those with elongated cells are *columnar epithelium.* Epithelium composed of a single layer of cells is called *simple;* whereas epithelium with two or more layers of cells is called *stratified.* In the following descriptions, note that the free surfaces of epithelial cells are modified in ways that reflect their specialized functions.

**PRACTICE**

3. List the general characteristics of epithelial tissue.
4. Describe the classification of epithelium in terms of cell shape and number of cell layers.

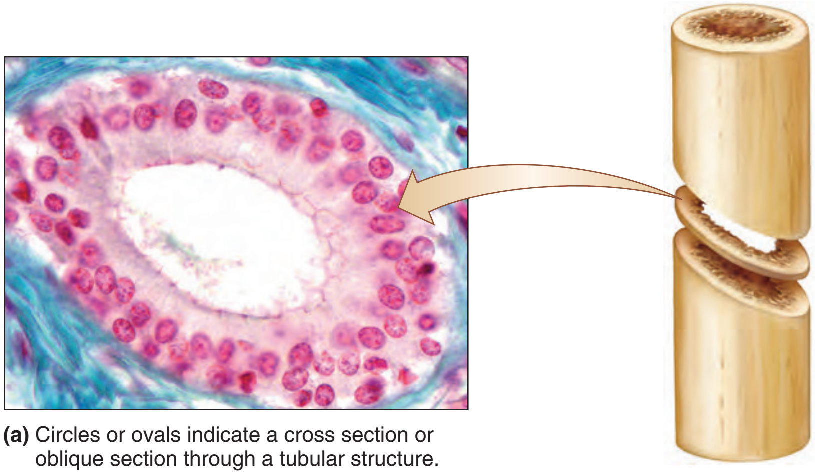
## Simple Squamous Epithelium

**Simple squamous** (skwa′mus) **epithelium** consists of a single layer of thin, flattened cells. These cells fit tightly together, somewhat like floor tiles, and their nuclei are usually broad and thin (fig. 5.2).

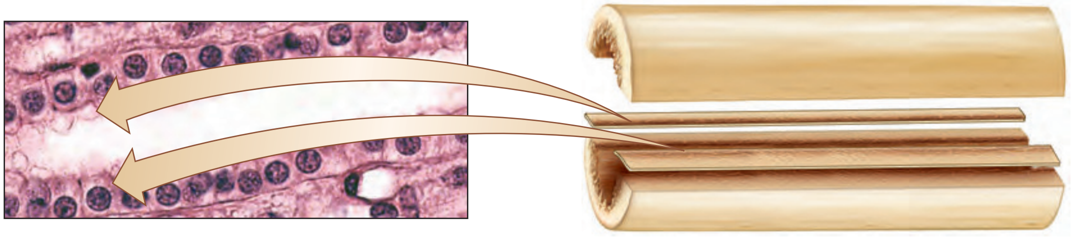
Substances pass rather easily through simple squamous epithelium, which is common at sites of diffusion

**TABLE 5.1 Tissues**

| Type | Function | Location | Distinguishing Characteristics |
|---|---|---|---|
| Epithelial | Protection, secretion, absorption, excretion | Cover body surface, cover and line internal organs, compose glands | Lack blood vessels, readily divide; cells are tightly packed |
| Connective | Bind, support, protect, fill spaces, store fat, produce blood cells | Widely distributed throughout body | Mostly have good blood supply; cells are farther apart than epithelial cells |
| Muscle | Movement | Attached to bones, in the walls of hollow internal organs, heart | Able to contract in response to specific stimuli |
| Nervous | Conduct impulses for coordination, regulation, integration, and sensory reception | Brain, spinal cord, nerves | Cells communicate with each other and other body parts |



**(a)** Circles or ovals indicate a cross section or oblique section through a tubular structure.



**(b)** Rows of cells with a space in between indicate a longitudinal section through a tube.

**FIGURE 5.1** Tissue sections. (**a**) Oblique section (600x). (**b**) Longitudinal section (165x).

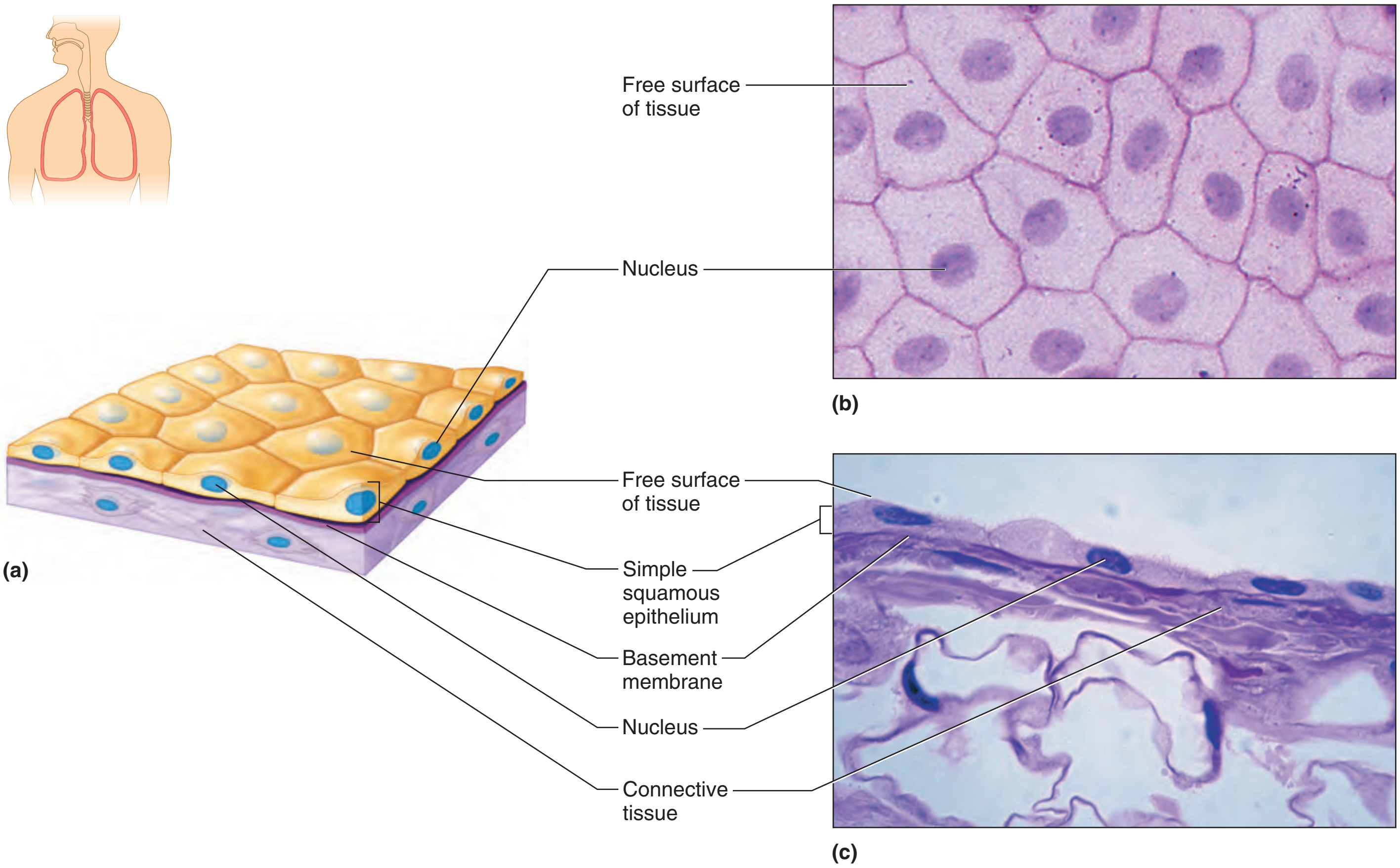


**FIGURE 5.2** Simple squamous epithelium consists of a single layer of tightly packed, flattened cells **(a)**. **(b)** Surface view (250x) and **(c)** side view (250x).

and filtration. For instance, simple squamous epithelium lines the air sacs (alveoli) of the lungs where oxygen and carbon dioxide are exchanged. It also forms the walls of capillaries, lines the insides of blood and lymph vessels, and is part of the membranes that line body cavities and cover the viscera. However, because it is so thin and delicate, simple squamous epithelium is easily damaged.

## Simple Cuboidal Epithelium

**Simple cuboidal epithelium** consists of a single layer of cube-shaped cells. These cells usually have centrally located, spherical nuclei (fig. 5.3).

Simple cuboidal epithelium covers the ovaries and lines most of the kidney tubules and the ducts of certain glands, where the free surface faces the hollow channel or *lumen*. In the kidneys, this tissue functions in secretion and absorption; in glands, it secretes glandular products.

## Simple Columnar Epithelium

The cells of **simple columnar epithelium** are longer than they are wide. This tissue is composed of a single layer of cells with elongated nuclei usually located at about the same level, near the basement membrane (fig. 5.4). The cells of this tissue can be ciliated or nonciliated. *Cilia* extend from the free surfaces of the cells and move constantly (see chapter 3, p. 68). In the female reproductive tract, cilia aid in moving the egg cell through the uterine tube to the uterus.

Nonciliated simple columnar epithelium lines the uterus and portions of the digestive tract, including the stomach and the small and large intestines. Because its cells are elongated, this tissue is thick, which enables it to protect underlying tissues. Simple columnar epithelium also secretes digestive fluids and absorbs nutrients from digested food.

Simple columnar cells, specialized for absorption, often have many tiny, cylindrical processes extending from their surfaces. These processes, called *microvilli,* increase the surface area of the cell membrane where it is exposed to substances being absorbed (fig. 5.4).

Typically, specialized flask-shaped glandular cells are scattered among the columnar cells of simple columnar epithelium. These cells, called *goblet cells,* secrete a protective fluid, called *mucus,* onto the free surface of the tissue (fig. 5.4).

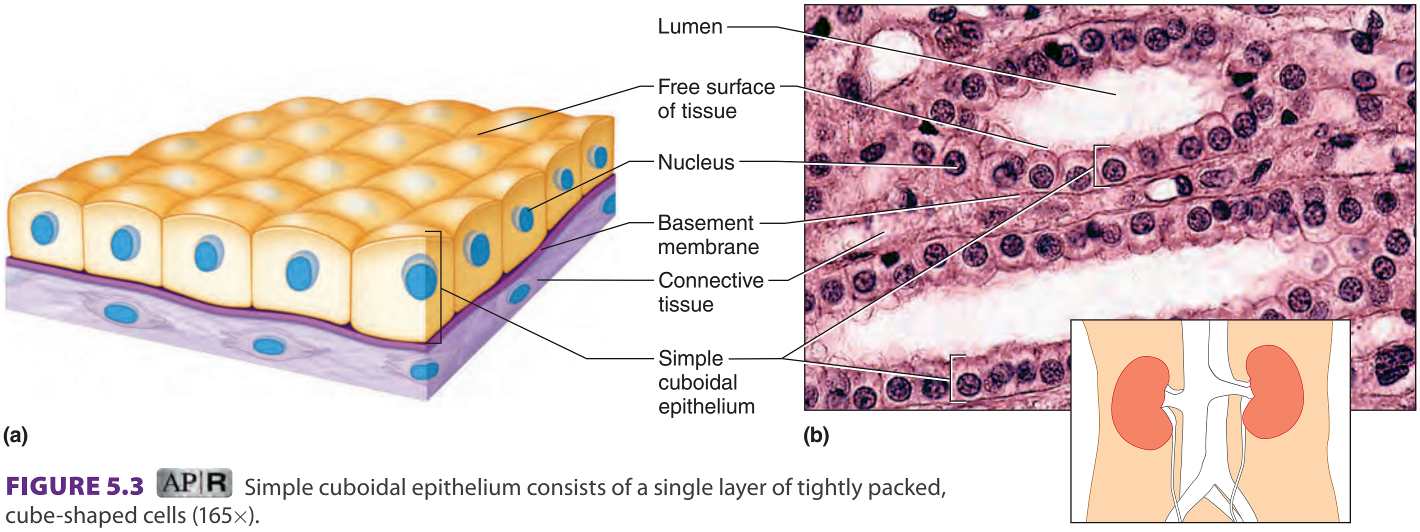

Lumen
Free surface of tissue
Nucleus
Basement membrane
Connective tissue
Simple cuboidal epithelium
(a)
(b)

**FIGURE 5.3** APR Simple cuboidal epithelium consists of a single layer of tightly packed, cube-shaped cells (165×).

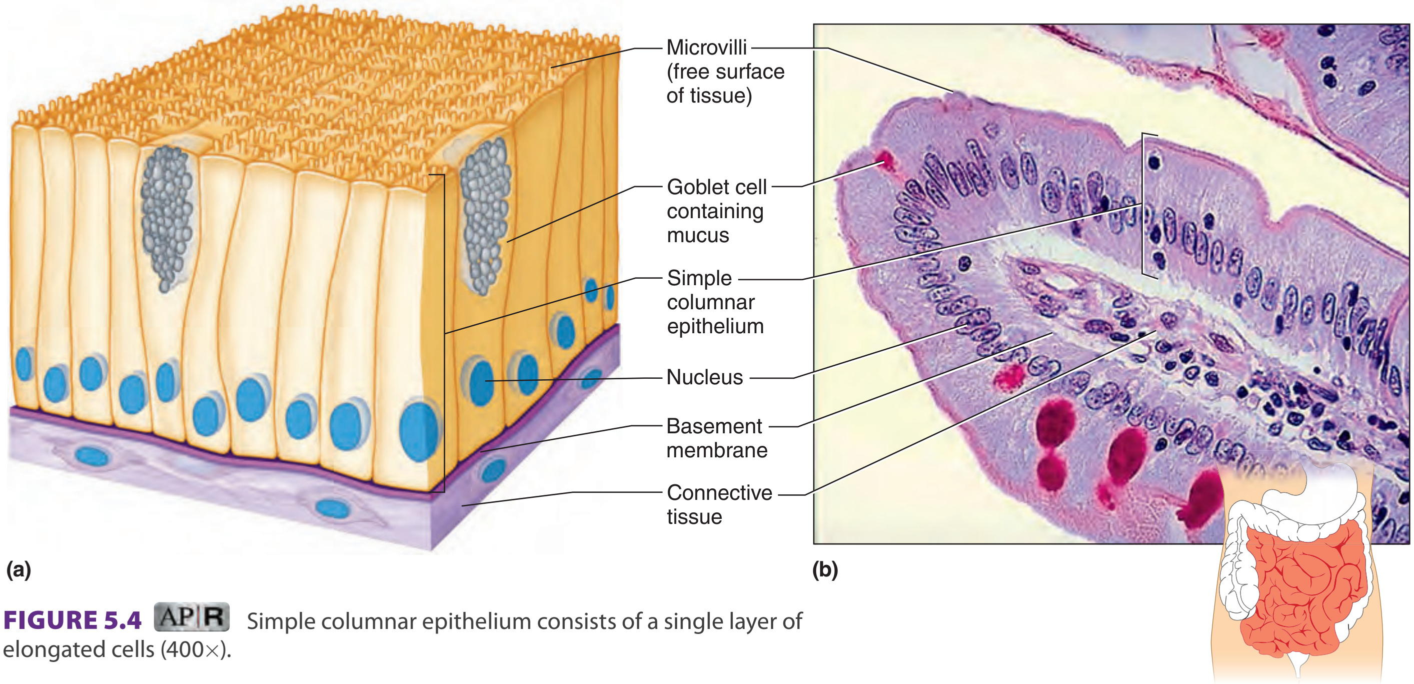

Microvilli (free surface of tissue)
Goblet cell containing mucus
Simple columnar epithelium
Nucleus
Basement membrane
Connective tissue
(a)
(b)

**FIGURE 5.4** APR Simple columnar epithelium consists of a single layer of elongated cells (400×).

## Pseudostratified Columnar Epithelium

The cells of **pseudostratified** (soo″do-strat′ĭ-fīd) **columnar epithelium** appear to be stratified or layered, but they are not. A layer effect occurs because the nuclei lie at two or more levels in the row of aligned cells. However, the cells, which vary in shape, all reach the basement membrane, even though some of them may not contact the free surface.

Pseudostratified columnar epithelial cells commonly have cilia, which extend from their free surfaces. Goblet cells scattered throughout this tissue secrete mucus, which the cilia sweep away (fig. 5.5).

Pseudostratified columnar epithelium lines the passages of the respiratory system. Here, the mucus-covered linings are sticky and trap dust and microorganisms that enter with the air. The cilia move the mucus and its captured particles upward and out of the airways.

## Stratified Squamous Epithelium

The many cell layers of **stratified squamous epithelium** make this tissue relatively thick. Cells divide in the deeper layers, and newer cells push older ones farther outward, where they flatten (fig. 5.6). In naming stratified epithelial tissues based on shape of cells, the appearance of the top layer of cells is used.

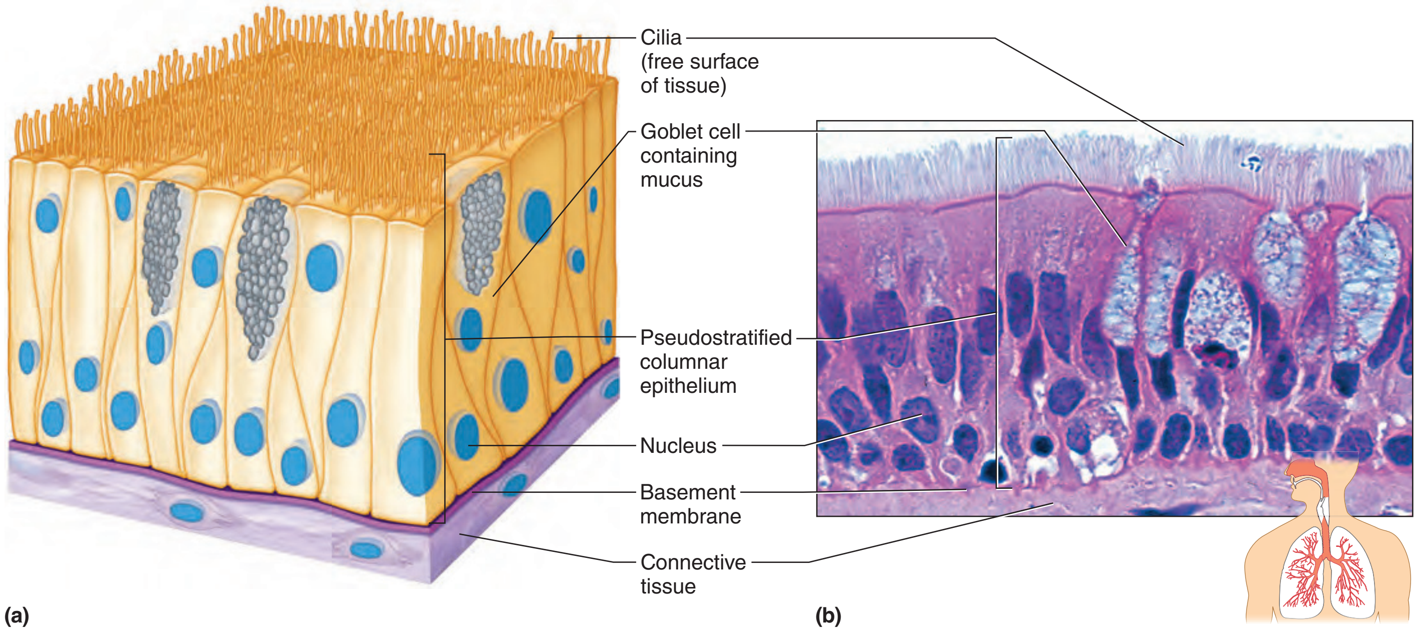

Cilia (free surface of tissue)
Goblet cell containing mucus
Pseudostratified columnar epithelium
Nucleus
Basement membrane
Connective tissue
(a)
(b)

**FIGURE 5.5** APR Pseudostratified columnar epithelium appears stratified because the cell nuclei are located at different levels (1,000×).

Stratified squamous epithelium forms the outermost layer of the skin (*epidermis*). As older skin cells are pushed outward, they accumulate a type of protein called *keratin,* and then harden and die. This "keratinization" produces a covering of dry, tough, protective material that prevents water and other substances from escaping underlying tissues and blocks chemicals and microorganisms from entering (see fig. 6.2, p. 130).

Stratified squamous epithelium also lines the oral cavity, esophagus, vagina, and anal canal. In these parts, the tissue is not keratinized; it stays soft and moist, and the cells on its free surfaces remain alive.

## Stratified Cuboidal Epithelium

**Stratified cuboidal epithelium** consists of two or three layers of cuboidal cells that form the lining of a lumen (fig. 5.7). The layering of the cells provides more protection than the single layer affords.

Stratified cuboidal epithelium lines the ducts of the mammary glands, sweat glands, salivary glands, and pancreas. It also forms the lining of developing ovarian follicles and seminiferous tubules, which are parts of the female and male reproductive systems, respectively.

## Stratified Columnar Epithelium

**Stratified columnar epithelium** consists of several layers of cells (fig. 5.8). The superficial cells are columnar, whereas the basal layers consist of cuboidal cells. Stratified columnar epithelium is found in part of the male urethra and lining the larger ducts of exocrine glands.

## Transitional Epithelium

**Transitional epithelium** is specialized to change in response to increased tension. It forms the inner lining of the urinary bladder and lines the ureters and the superior urethra. When the wall of one of these organs contracts, the tissue consists of several layers of irregular-shaped cells; when the organ is distended, however, the tissue stretches, and the cells elongate (fig. 5.9). In addition to providing an expandable lining, transitional epithelium forms a barrier that helps prevent the contents of the urinary tract from diffusing back into the internal environment.

Up to 90% of all human cancers are *carcinomas,* growths that originate in epithelium. Most carcinomas begin on surfaces that contact the external environment, such as skin, linings of the airways, or linings of the stomach or intestine. This observation suggests that the more common cancer-causing agents may not deeply penetrate tissues. Carcinomas may also arise internally, such as in a duct in a breast or in the prostate gland.

## Glandular Epithelium

**Glandular epithelium** is composed of cells specialized to produce and secrete substances into ducts or into body fluids. Such cells are usually found within columnar or cuboidal epithelium, and one or more of these cells constitute a *gland.* Glands that secrete their products into ducts that open onto surfaces, such as

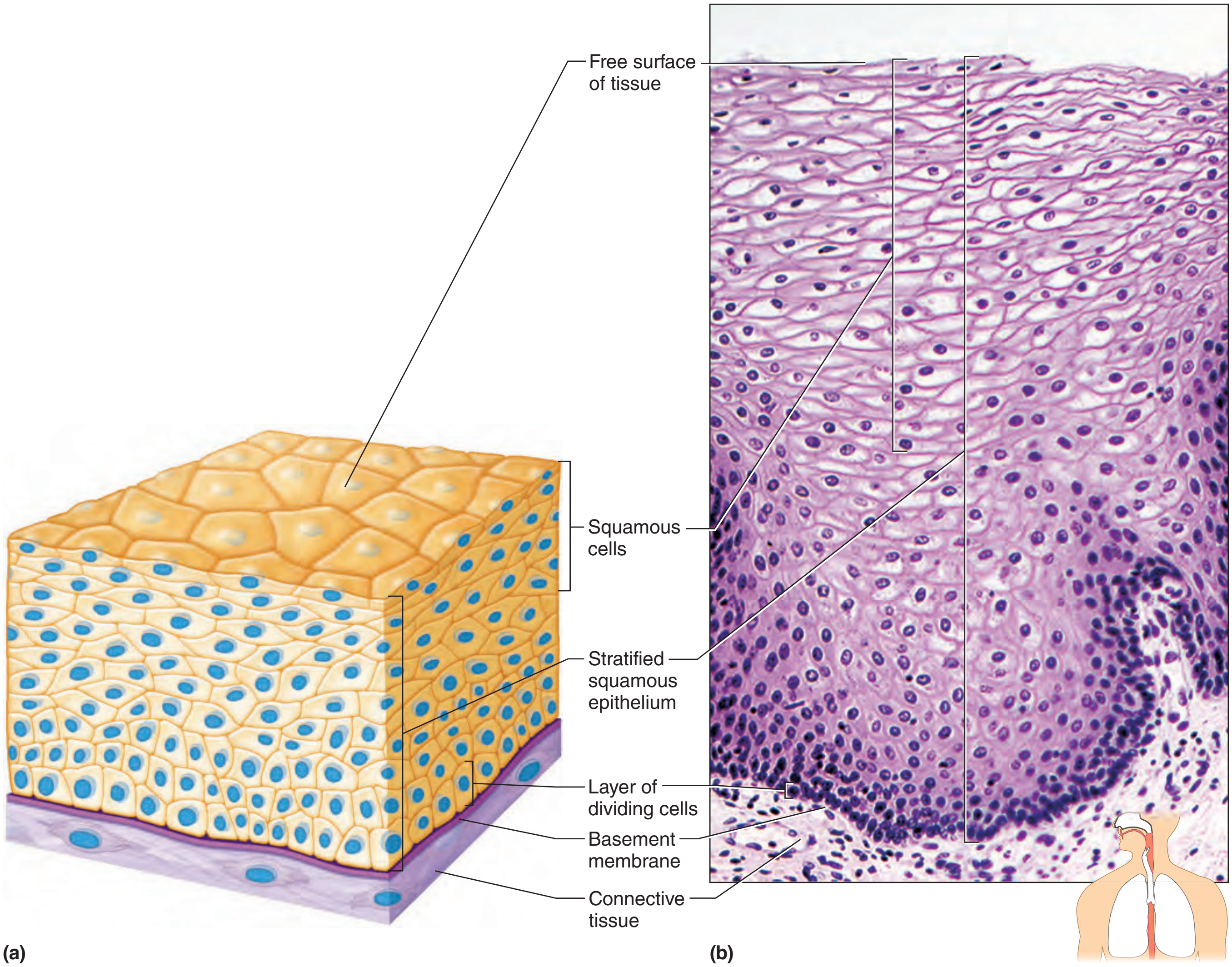

Free surface of tissue
Squamous cells
Stratified squamous epithelium
Layer of dividing cells
Basement membrane
Connective tissue
(a)
(b)

**FIGURE 5.6** APIR Stratified squamous epithelium consists of many layers of cells (65×).

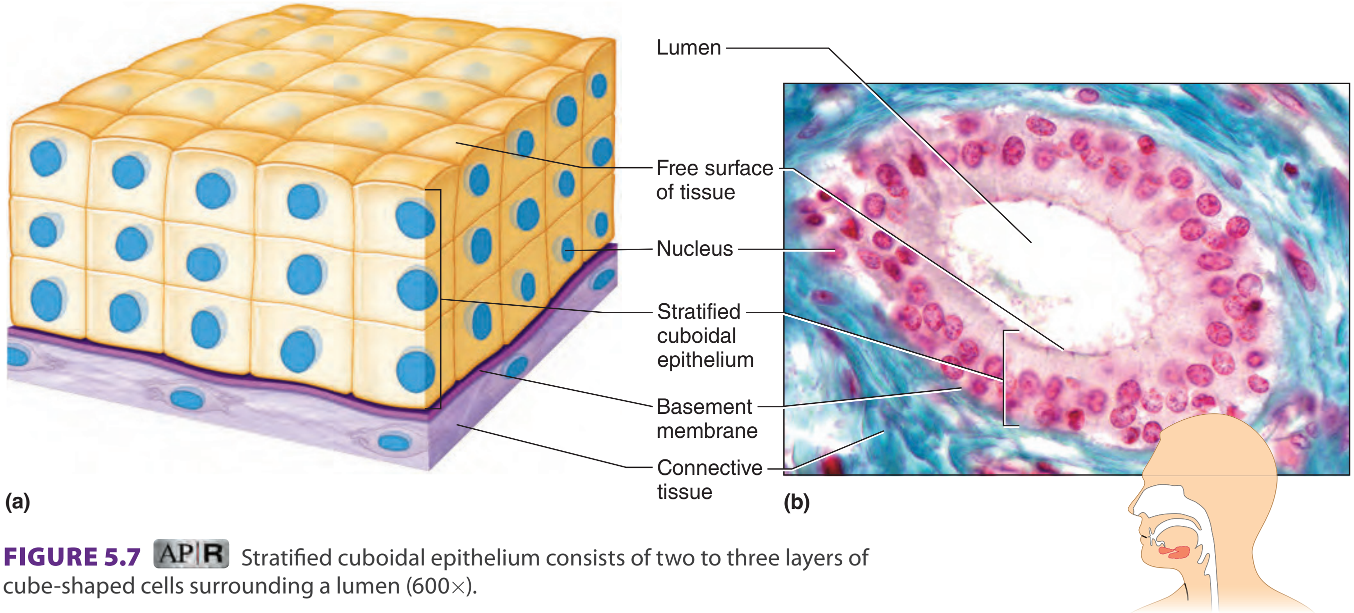

Lumen
Free surface of tissue
Nucleus
Stratified cuboidal epithelium
Basement membrane
Connective tissue
(a)
(b)

**FIGURE 5.7** APIR Stratified cuboidal epithelium consists of two to three layers of cube-shaped cells surrounding a lumen (600×).

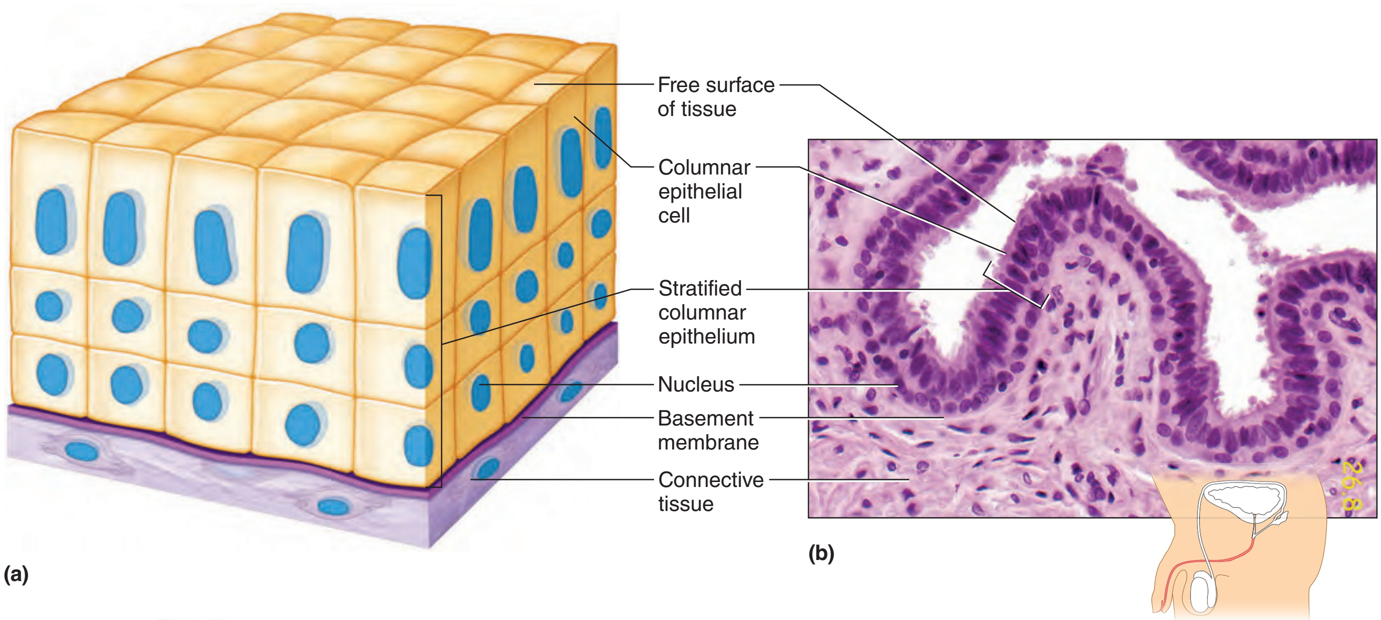


**FIGURE 5.8** APR Stratified columnar epithelium consists of a superficial layer of columnar cells overlying several layers of cuboidal cells (230×).

Q *In the micrograph (b), is this section through the urethra a cross section or a longitudinal section?*
**Answer can be found in Appendix F on page 582.**

the skin or the lining of the digestive tract, are called **exocrine glands.** Glands that secrete their products into tissue fluid or blood are called **endocrine glands.** (Endocrine glands are discussed in chapter 11.)

Exocrine glands are classified according to the ways these glands secrete their products (fig. 5.10). Glands that release fluid by exocytosis are called **merocrine** (mer′o-krin) **glands.** Glands that lose small portions of their glandular cell bodies during secretion are called **apocrine** (ap′o-krin) **glands.** Glands that release entire cells that disintegrate to release cell secretions are called **holocrine** (ho′lo-krin) **glands.** Table 5.2 summarizes these glands and their secretions.

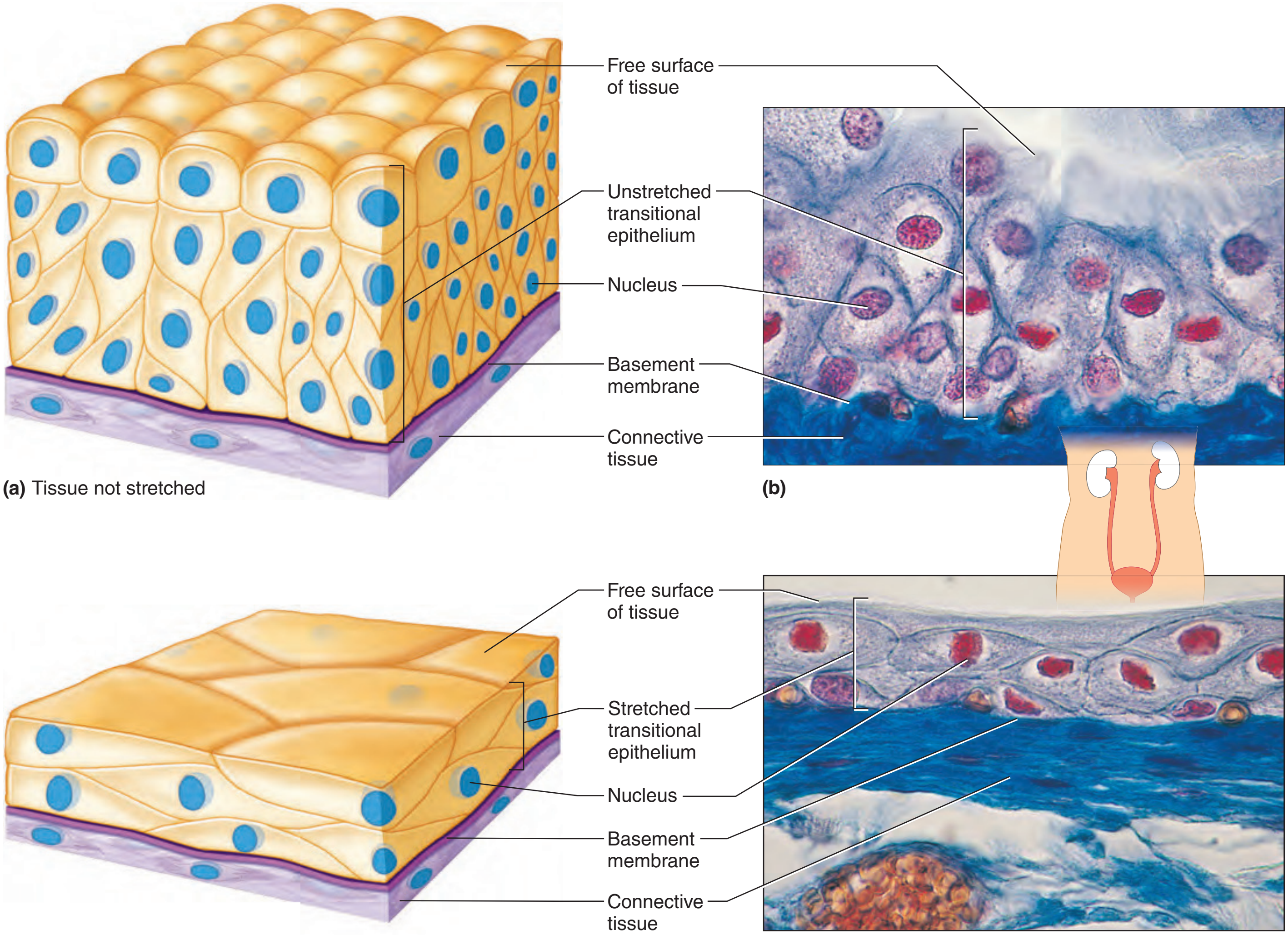
Most exocrine secretory cells are merocrine, and they can be further subclassified based on their secretion of serous fluid or mucus. *Serous fluid* is typically watery, and has a high concentration of enzymes. Serous cells secreting this fluid, which lubricates, are commonly associated with the visceral and parietal membranes of the thoracic and abdominopelvic cavities. The thicker fluid, *mucus,* is rich in the glycoprotein *mucin* and abundantly secreted by cells, for protection, in the inner linings of the digestive, respiratory, and reproductive systems. Mucous cells and goblet cells secrete mucus, but in different parts of the body. Table 5.3 summarizes the characteristics of the different types of epithelial tissues.

## PRACTICE

5. Describe the special functions of each type of epithelium.
6. Distinguish between exocrine glands and endocrine glands.
7. Explain how exocrine glands are classified.
8. Distinguish between serous fluid and mucus.

**TABLE 5.2 Exocrine Glandular Secretions**

| Type of Gland | Description of Secretion | Example |
|---|---|---|
| Merocrine glands | A fluid product released through the cell membrane by exocytosis | Salivary glands, pancreatic glands, sweat glands of the skin |
| Apocrine glands | Cellular product and portions of the free ends of glandular cells pinch off during secretion | Mammary glands, ceruminous glands lining the external ear canal |
| Holocrine glands | Disintegrated entire cells filled with secretory products | Sebaceous glands of the skin |


Free surface of tissue
Unstretched transitional epithelium
Nucleus
Basement membrane
Connective tissue
Free surface of tissue
Stretched transitional epithelium
Nucleus
Basement membrane
Connective tissue

**(a)** Tissue not stretched

**(b)**

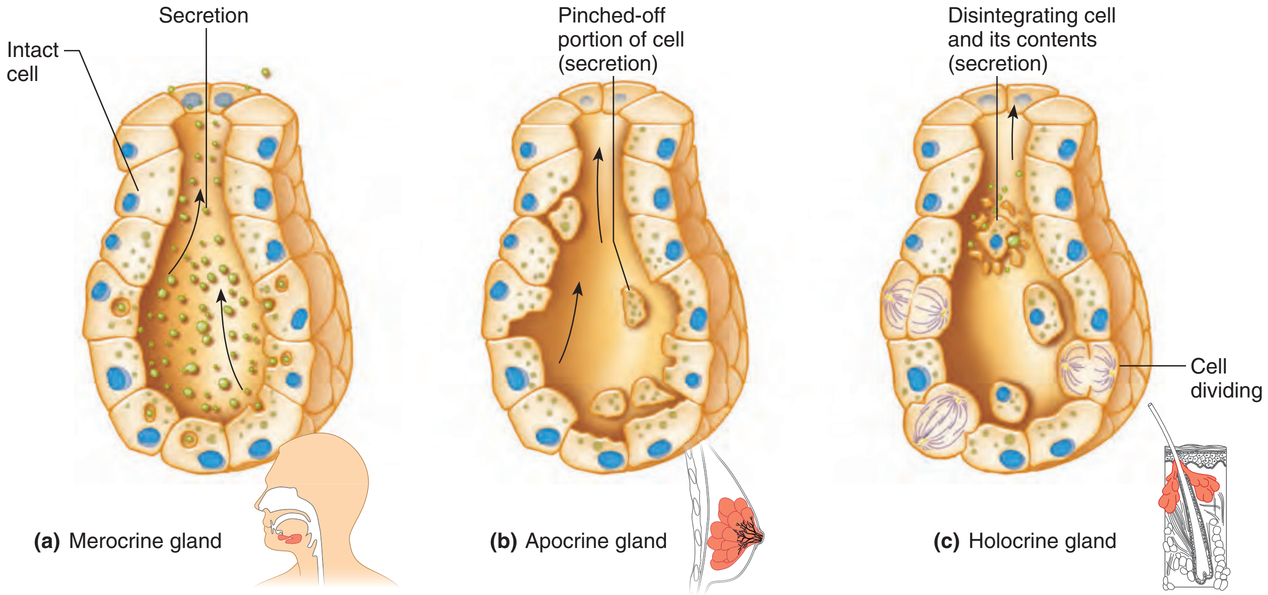
**(c)** Tissue stretched

**(d)**

**FIGURE 5.9** APR Transitional epithelium. (**a** and **b**) When the organ wall contracts, transitional epithelium is unstretched and consists of many layers (675×). (**c** and **d**) When the organ is distended, the tissue stretches and appears thinner (675×).

**TABLE 5.3 Epithelial Tissues**

| Type | Function | Location |
|---|---|---|
| Simple squamous epithelium | Filtration, diffusion, osmosis; covers surface | Air sacs of the lungs, walls of capillaries, linings of blood and lymph vessels, part of the membranes lining body cavities and covering viscera |
| Simple cuboidal epithelium | Secretion, absorption | Surface of ovaries, linings of kidney tubules, and linings of ducts of certain glands |
| Simple columnar epithelium | Protection, secretion, absorption | Linings of uterus, stomach, and intestines |
| Pseudostratified columnar epithelium | Protection, secretion, movement of mucus | Linings of respiratory passages |
| Stratified squamous epithelium | Protection | Outer layer of skin, and linings of oral cavity, throat, vagina, and anal canal |
| Stratified cuboidal epithelium | Protection | Linings of ducts of mammary glands, sweat glands, salivary glands, and pancreas |
| Stratified columnar epithelium | Protection, secretion | Part of the male urethra and linings of larger ducts of excretory glands |
| Transitional epithelium | Distensibility, protection | Inner lining of urinary bladder and linings of ureters and part of urethra |
| Glandular epithelium | Secretion | Salivary glands, sweat glands, endocrine glands |


Secretion
Intact cell
Pinched-off portion of cell (secretion)
Disintegrating cell and its contents (secretion)
Cell dividing

**(a)** Merocrine gland **(b)** Apocrine gland **(c)** Holocrine gland

**FIGURE 5.10** Types of exocrine glands. **(a)** APR Merocrine glands release secretions without losing cytoplasm. **(b)** APR Apocrine glands lose small portions of their cell bodies during secretion. **(c)** APR Holocrine glands release entire cells filled with secretory products.

## 5.3 | Connective Tissues APR

### General Characteristics

**Connective** (kŏ-nek′tiv) **tissues** bind structures, provide support and protection, serve as frameworks, fill spaces, store fat, produce blood cells, protect against infections, and help repair tissue damage. Connective tissue cells are farther apart than epithelial cells, and they have abundant **extracellular matrix** (eks″trah-sel′u-lar ma′triks) between them. This extracellular matrix is composed of *protein fibers,* and a *ground substance* consisting of nonfibrous protein and other molecules, and fluid. The consistency of the extracellular matrix varies from fluid to semisolid to solid. Some connective tissues, such as bone and cartilage, are quite rigid. Loose connective tissue and dense connective tissue are more flexible. Clinical Application 5.1 discusses the extracellular matrix and its relationship to disease.

Most connective tissue cells can divide. In most cases connective tissues have good blood supplies and are well nourished, but the density of blood vessels (vascularity) varies.

### *Major Cell Types*

Connective tissues contain a variety of cell types. Some cells are called *fixed cells* because they reside in the tissue for an extended period of time. These include fibroblasts and mast cells. Other cells, such as macrophages, are *wandering cells.* They move through and appear in tissues temporarily, usually in response to an injury or infection.

**Fibroblasts** (fi′bro-blastz) are the most common type of fixed cell in connective tissue. These large, star-shaped cells produce fibers by secreting proteins into the extracellular matrix of connective tissues (fig. 5.11).

**Macrophages** (mak′ro-fājez), or histiocytes, originate as white blood cells (see chapter 12, p. 334) and are almost as numerous as fibroblasts in some connective tissues. Macrophages are specialized to carry on phagocytosis. They can move about and clear foreign particles from tissues (fig. 5.12).

**Mast cells** are large and widely distributed in connective tissues. They are usually near blood vessels (fig. 5.13). Mast cells release *heparin,* a compound that prevents blood clotting, and *histamine,* a substance that promotes some of the reactions associated with inflammation and allergies (see chapter 14, p. 403).

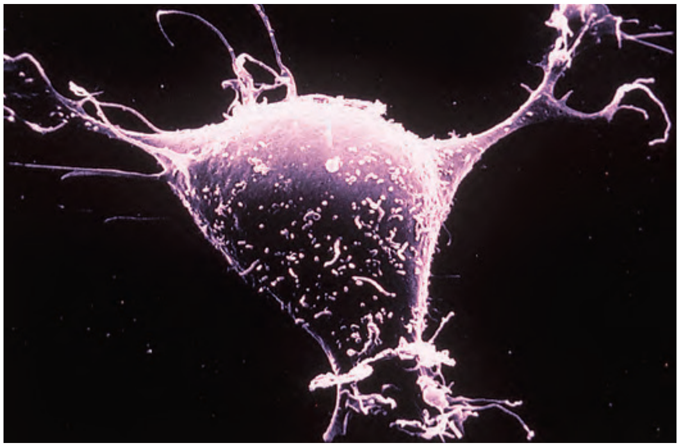


**FIGURE 5.11** Scanning electron micrograph of a fibroblast (4,000×), the most abundant cell type of connective tissue.

## CLINICAL APPLICATION 5.1

## The Body's Glue: The Extracellular Matrix (ECM)

Rather than being just "filler" between cells, the extracellular matrix (ECM) is a complex and changing mix of molecules that modifies the tissue to suit different organs and conditions. Not only does the ECM serve as a scaffolding to organize cells into tissues, but it relays the biochemical signals that control cell division, cell differentiation, tissue repair, and cell migration.

The ECM has two basic components: the basement membrane that anchors epithelium to underlying connective tissue, and the rest of the material between cells, called the interstitial matrix. The basement membrane is mostly composed of tightly packed collagen fibers from which large, cross-shaped glycoproteins called laminins extend. The laminins (and other glycoproteins such as fibronectin, the proteoglycans, and tenascin) traverse the interstitial matrix and contact receptors, called integrins, on other cells (fig. 5A). In this way, the ECM connects cells into tissues. At least twenty types of collagen and precursors of hormones, enzymes, growth factors, and immune system biochemicals (cytokines) compose the various versions of the ECM. The precursor molecules are activated under certain conditions.

The components of the ECM are always changing, as its cells synthesize proteins while enzymes called proteases break down specific proteins. The balance of components is important to maintaining and repairing organ structure. Disrupt the balance, and disease can result. Following are three common examples.

### Cancer

The spread of a cancerous growth takes advantage of the normal ability of fibroblasts to contract as they close a wound, where they are replaced with normal epithelium. Chemical signals from cancer cells make fibroblasts more contractile, and they take on the characteristics of cancer cells. At the same time, alterations in laminins loosen the connections of the fibroblasts to surrounding cells. This abnormal flexibility enables the changed fibroblasts to migrate, helping the cancer spread.

### Liver Fibrosis

In fibrosis, which is a part of all chronic liver diseases, collagen deposition increases so that the ECM exceeds its normal 3% of the organ. Healthy liver ECM sculpts a framework that supports the epithelial and vascular tissues of the organ. In response to a damaging agent such as a virus, alcohol, or a toxic drug, hepatic stellate cells secrete collagen fibers in the areas where the epithelium and blood vessels meet. Such limited fibrosis seals off the affected area, preventing spread of the damage. But if the process continues—if an infection is not treated or the noxious stimulus not removed—the ECM grows and eventually blocks the interaction between liver cells and the bloodstream. The liver tissue can harden, in a dangerous condition called *cirrhosis*.

### Heart Failure and Atherosclerosis

The heart's ECM organizes cells into a three-dimensional network that coordinates their contractions into the rhythmic heartbeat necessary to pump blood. This ECM consists of collagen, fibronectin, laminin, and elastin surrounding cardiac muscle cells and myofibroblasts, and is also in the walls of arteries. Some forms of heart failure reflect imbalances of collagen production and degradation. In heart muscle, as in the liver, the natural response of ECM buildup is to wall off an area where circulation is blocked, but if it continues, the extra scaffolding stiffens the heart, which can lead to heart failure. During a myo-

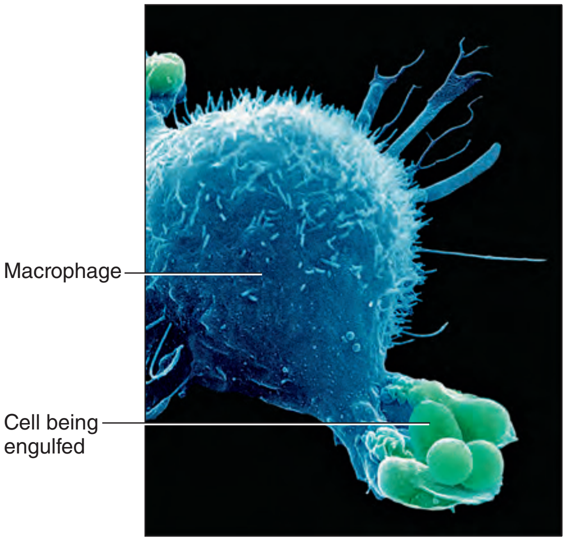


**FIGURE 5.12** Macrophages are scavenger cells common in connective tissues. This scanning electron micrograph shows a macrophage engulfing bacteria (3,300×).

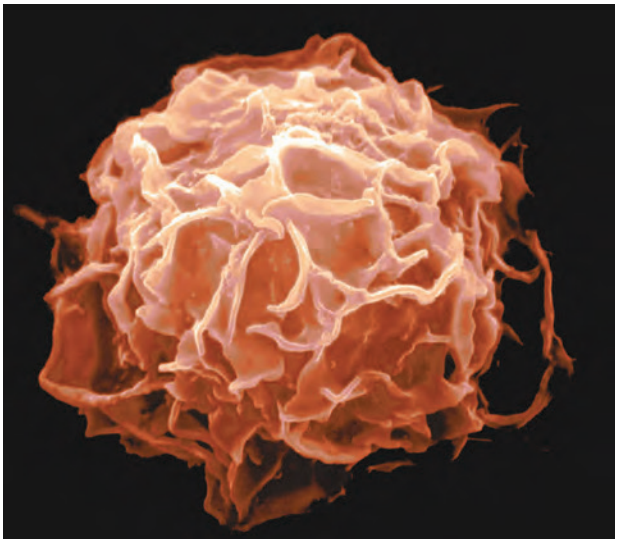


**FIGURE 5.13** Scanning electron micrograph of a mast cell (6,600×), which releases heparin and histamine.

cardial infarction (heart attack), collagen synthesis and deposition increase in affected and nonaffected heart parts, which is why damage can continue even after pain stops. In atherosclerosis, excess ECM accumulates on the interior linings of arteries, blocking blood flow. Collagen accumulation is also associated with atherosclerosis.

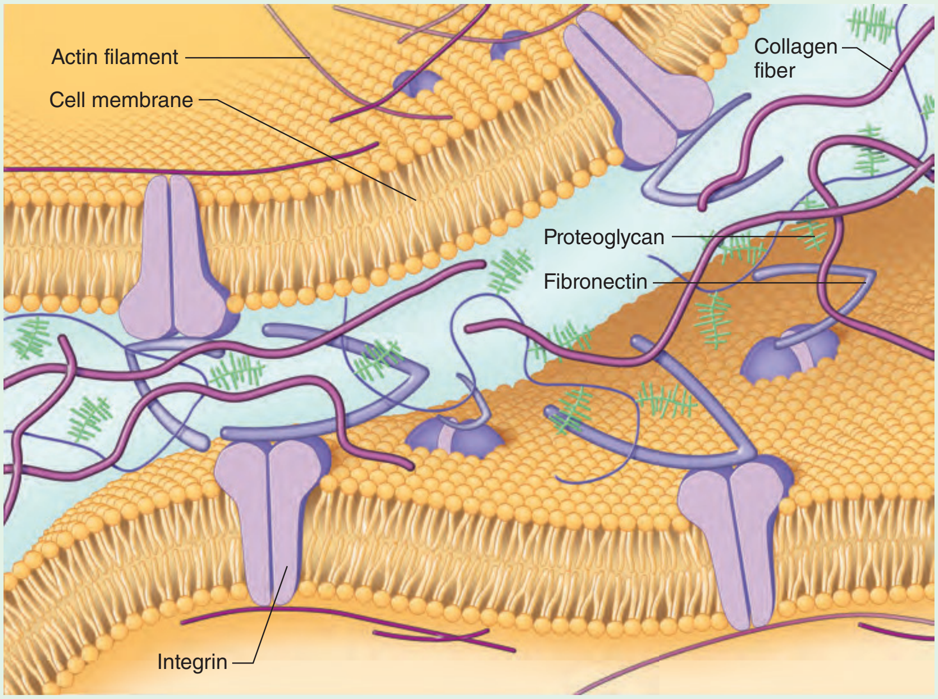


**FIGURE 5A** The extracellular matrix (ECM) is a complex and dynamic meshwork of various proteins and glycoproteins. Collagen is abundant. Other common components include integrins that anchor the ECM to cells, proteoglycans, and fibronectin. The ECM may also include precursors of growth factors, hormones, enzymes, and cytokines. It is vital to maintaining the specialized characteristics of tissues and organs.

### *Connective Tissue Fibers*

Fibroblasts produce three types of connective tissue fibers: collagen fibers, elastic fibers, and reticular fibers. Of these, collagen and elastic fibers are the most abundant.

**Collagen** (kol′ah-jen) **fibers** are thick threads of the protein *collagen*. They are grouped in long, parallel bundles, and are flexible but only slightly elastic. More importantly, they have great tensile strength—that is, they resist considerable pulling force. Thus, collagen fibers are important components of body parts that hold structures together, such as **ligaments** (which connect bones to bones) and **tendons** (which connect muscles to bones).

Tissue containing abundant collagen fibers is called *dense connective tissue*. It appears white, and for this reason collagen fibers are sometimes called *white fibers*. In contrast, *loose connective tissue* has fewer collagen fibers.

**Elastic fibers** are composed of a springlike protein called *elastin*. These thin fibers branch, forming complex networks. Elastic fibers are weaker than collagen fibers, but they are easily stretched or deformed and will resume their original lengths and shapes when the force acting on them is removed. Elastic fibers are abundant in body parts normally subjected to stretching, such as the vocal cords. They are also called *yellow fibers* because tissues well supplied with them appear yellowish.

**Reticular fibers** are thin collagen fibers. They are highly branched and form delicate supporting networks in a variety of tissues, including those of the spleen. Table 5.4 summarizes the components of connective tissue, and their functions.

When skin is exposed to prolonged and intense sunlight, connective tissue fibers lose elasticity, and the skin stiffens and becomes leathery. In time, the skin may sag and wrinkle. Collagen injections may temporarily smooth out wrinkles. However, collagen applied as a cream to the skin does not combat wrinkles because collagen molecules are far too large to penetrate the skin.

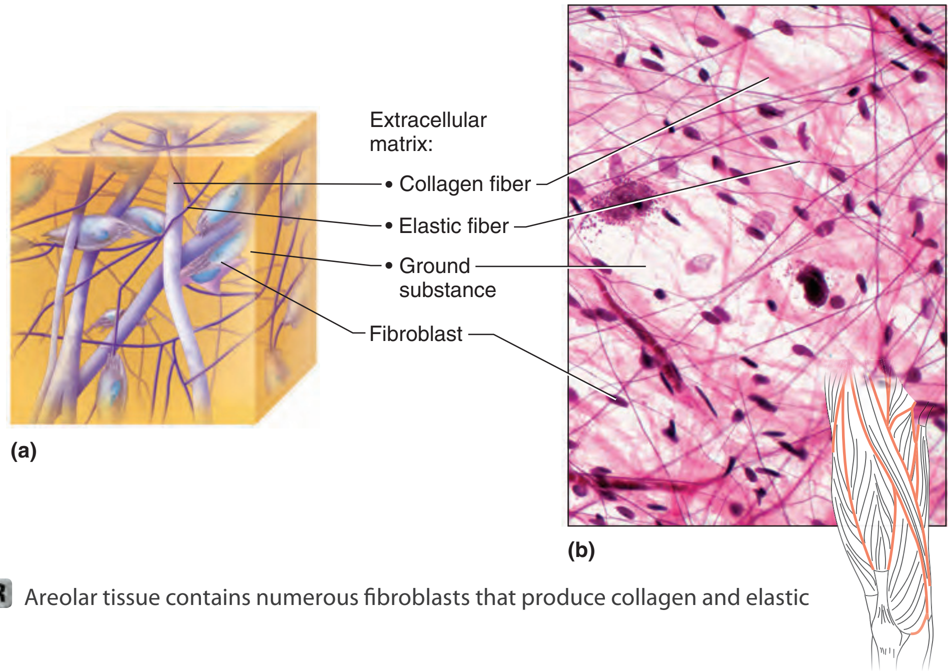


**FIGURE 5.14** Areolar tissue contains numerous fibroblasts that produce collagen and elastic fibers (800×).

## Categories of Connective Tissue

Connective tissue is divided into two major categories. *Connective tissue proper* includes loose connective tissue and dense connective tissue. The *specialized connective tissues* include cartilage, bone, and blood.

### *Loose Connective Tissue*

**Loose connective tissue** includes areolar tissue, adipose tissue, and reticular connective tissue. **Areolar** (ah-re′o-lar) **tissue** forms delicate, thin membranes throughout the body. The cells of this tissue, mainly fibroblasts, are located some distance apart and are separated by a gel-like ground substance that contains many collagen and elastic fibers that fibroblasts secrete (fig. 5.14). Areolar tissue binds the skin to the underlying organs and fills spaces between muscles. It lies beneath most layers of epithelium, where its many blood vessels nourish nearby epithelial cells.

**TABLE 5.4 Components of Connective Tissue**

| Component | Function |
|---|---|
| Celluar | |
| Fibroblasts | Produce fibers |
| Macrophages | Carry on phagocytosis |
| Mast cells | Secrete heparin and histamine |
| Extracellular (matrix) | |
| Collagen fibers | Hold structures together with great tensile strength |
| Elastic fibers | Stretch easily |
| Reticular fibers | Lend delicate support |
| Ground substance | Fills in spaces around cells and fibers |

**Adipose** (ad′ĭ-pōs) **tissue,** or fat, develops when certain cells (adipocytes) store fat as droplets in their cytoplasm and enlarge (fig. 5.15). When such cells become so abundant that they crowd other cell types, they form adipose tissue. Adipose tissue lies beneath the skin, in spaces between muscles, around the kidneys, behind the eyeballs, in certain abdominal membranes, on the surface of the heart, and around certain joints. Adipose tissue cushions joints and some organs, such as the kidneys. It also insulates beneath the skin, and it stores energy in fat molecules.

Overeating and lack of exercise can increase the size of adipose cells, leading to being overweight or obese. During periods of fasting, however, fat supplies energy, and adipocytes lose fat, shrink, and become more like fibroblasts.

**Reticular connective tissue** is composed of thin, collagen fibers in a three-dimensional network. It helps provide the framework of certain internal organs, such as the liver and spleen.

### *Dense Connective Tissue*

**Dense connective tissue** consists of many closely packed, thick, collagen fibers and a fine network of elastic fibers. It has few cells, most of which are fibroblasts (fig. 5.16).

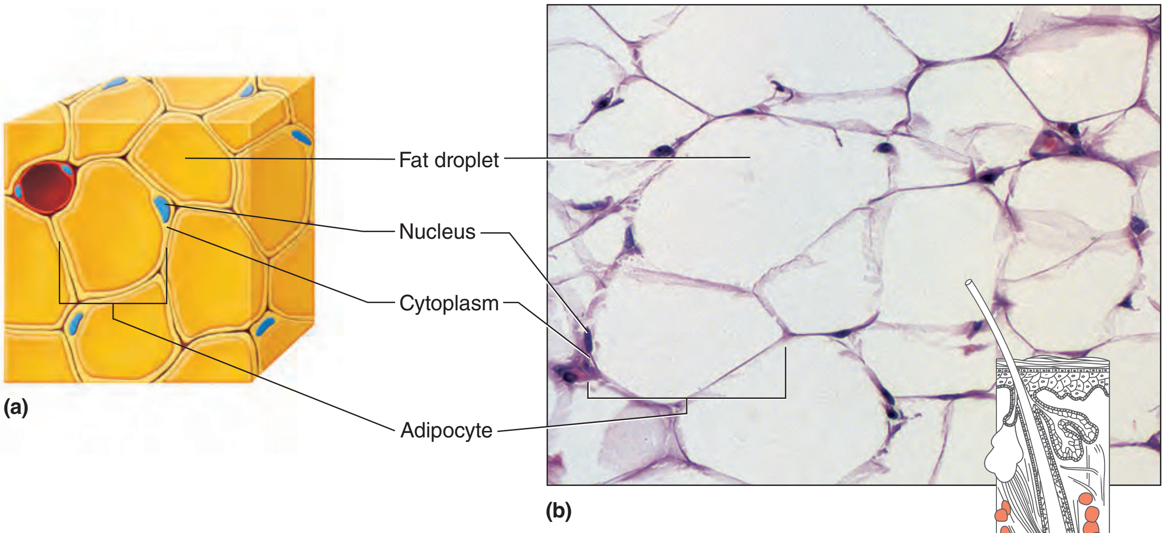


**FIGURE 5.15** APR Adipose tissue cells contain large fat droplets that push the nuclei close to the cell membranes (400×).

Collagen fibers of dense connective tissue are very strong, enabling the tissue to withstand pulling forces. It often binds body structures as part of tendons and ligaments. This type of tissue is also in the protective white layer of the eyeball and in the deeper skin layers. The blood supply to dense connective tissue is poor, slowing tissue repair.

## PRACTICE

9. What are the general characteristics of connective tissues?
10. What are the characteristics of collagen and elastin?
11. What feature distinguishes adipose tissue from other connective tissues?
12. Explain the difference between loose connective tissue and dense connective tissue.

### *Cartilage*

**Cartilage** (kar′ti-lij) is a rigid connective tissue. It provides support, frameworks, and attachments, protects underlying tissues, and forms structural models for many developing bones.

Cartilage extracellular matrix is abundant and is largely composed of collagen fibers embedded in a gel-like ground substance. Cartilage cells, or **chondrocytes** (kon′dro-sītz), occupy small chambers called *lacunae* and lie completely within the extracellular matrix (fig. 5.17).

A cartilaginous structure is enclosed in a covering of connective tissue called the *perichondrium.* Nutrients diffuse to cartilage cells from blood vessels in the perichondrium. Because this tissue does not have a direct blood supply, cartilage heals slowly and chondrocytes do not divide frequently.

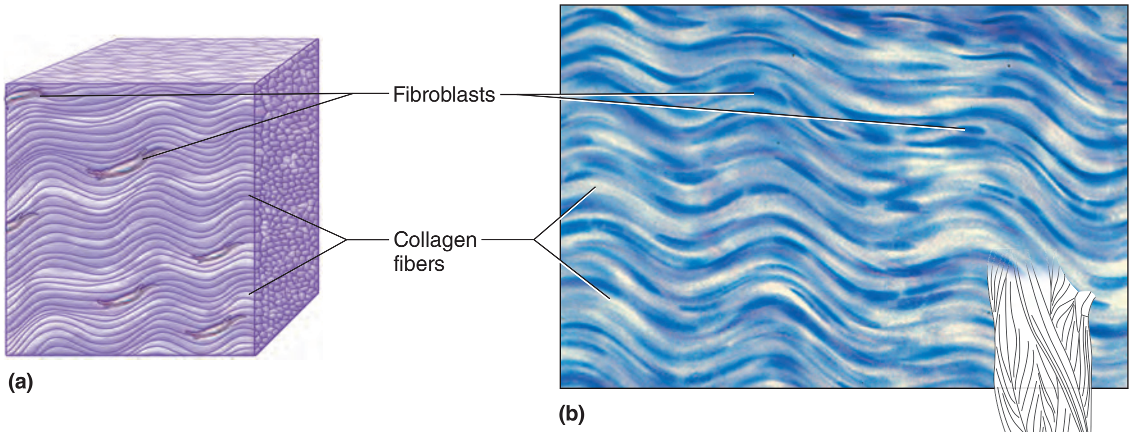


**FIGURE 5.16** APR Dense connective tissue consists largely of tightly packed collagen fibers (500×).

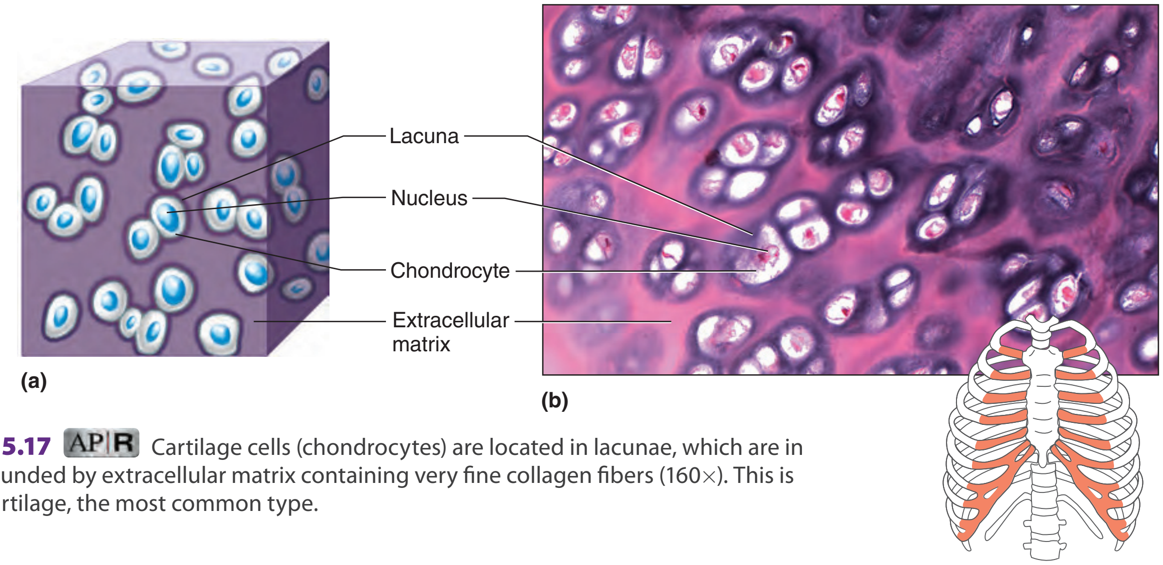


**FIGURE 5.17** APR Cartilage cells (chondrocytes) are located in lacunae, which are in turn surrounded by extracellular matrix containing very fine collagen fibers (160×). This is hyaline cartilage, the most common type.

Different types of extracellular matrix distinguish three types of cartilage. **Hyaline cartilage,** the most common type, has very fine collagen fibers in its extracellular matrix and looks somewhat like white glass (fig. 5.17). It is found on the ends of bones in many joints, in the soft part of the nose, and in the supporting rings of the respiratory passages. Hyaline cartilage is also important in the development and growth of most bones (see chapter 7, p. 147).

**Elastic cartilage** has a dense network of elastic fibers and thus is more flexible than hyaline cartilage (fig. 5.18). It provides the framework for the external ears and for parts of the larynx.

**Fibrocartilage,** a very tough tissue, has many collagen fibers (fig. 5.19). It is a shock absorber for structures that are subjected to pressure. For example, fibrocartilage forms pads (intervertebral discs) between the individual bones (vertebrae) of the spinal column. It also cushions bones in the knees and in the pelvic girdle.

**FACTS OF LIFE** Between ages thirty and seventy, a person's nose may lengthen and widen by as much as half an inch, and the ears may lengthen by a quarter inch, because the cartilage in these areas continues to grow as we age.

### *Bone*

**Bone** is the most rigid connective tissue. Its hardness is largely due to mineral salts, such as calcium phosphate and calcium carbonate, between cells. This extracellular matrix also has many collagen fibers, which are flexible and reinforce the mineral components of bone.

Bone internally supports body structures. It protects vital parts in the cranial and thoracic cavities, and is an attachment for muscles. Bone also contains red marrow,

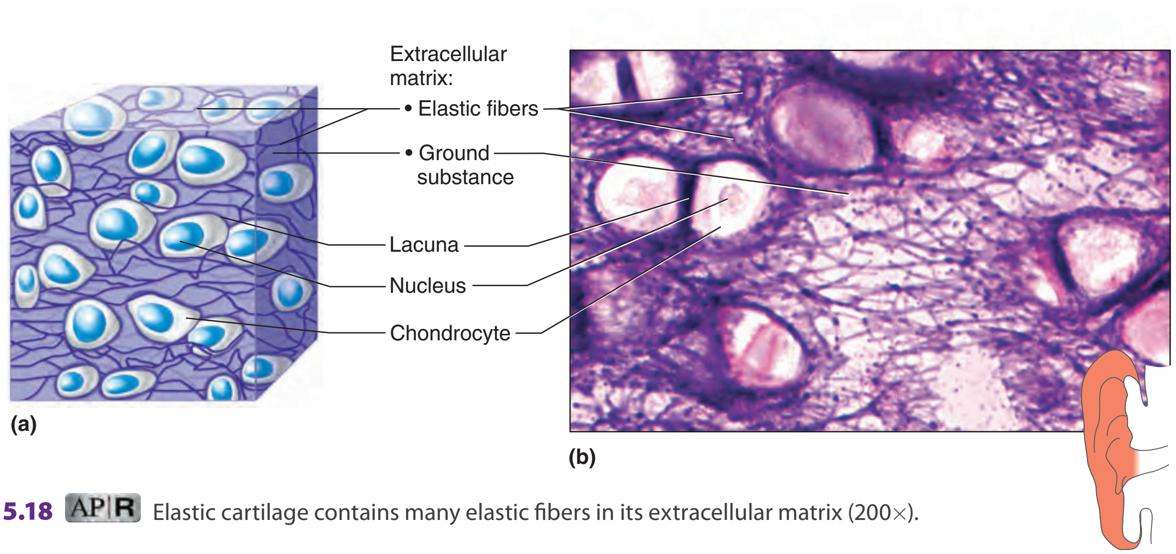


**FIGURE 5.18** APR Elastic cartilage contains many elastic fibers in its extracellular matrix (200×).

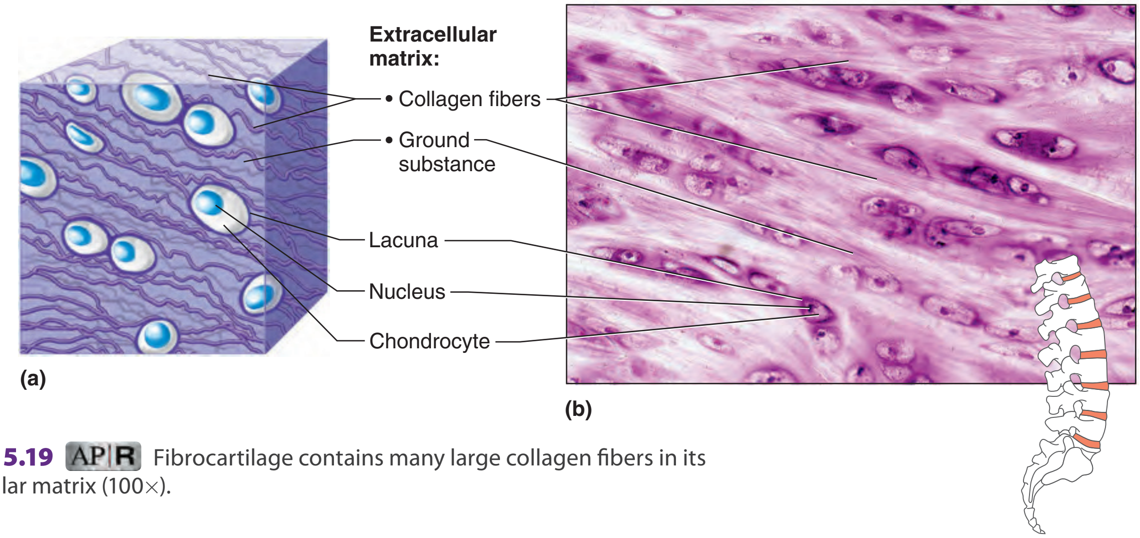


**FIGURE 5.19** APR Fibrocartilage contains many large collagen fibers in its extracellular matrix (100×).

which forms blood cells. It stores and releases inorganic chemicals such as calcium and phosphorus.

Bone matrix is deposited in thin layers called *lamellae,* which form concentric patterns around tiny longitudinal tubes called *central canals,* or Haversian canals (fig. 5.20). Bone cells, or **osteocytes** (os′te-o-sītz), are located in lacunae, which are rather evenly spaced within the lamellae.

In a bone, the osteocytes and layers of extracellular matrix, which are concentrically clustered around a central canal, form a cylinder-shaped unit called an **osteon** (os′te-on), or Haversian system. Many osteons cemented together form the substance of compact bone.

Each central canal contains a blood vessel, which places every bone cell near a nutrient supply. In addition, bone cells have many cytoplasmic processes that extend outward and pass through very small tubes in the extracellular matrix called *canaliculi.* These cellular processes connect with the processes of nearby cells. As a result, materials can move rapidly between blood vessels and bone cells. Thus, in spite of its inert appearance, bone is a very active tissue that heals much more rapidly than does injured cartilage. (The microscopic structure of bone is described in more detail in chapter 7, pp. 145–146.)

### *Blood*

**Blood** transports a variety of materials between interior body cells and those that exchange substances with the external environment. In this way, blood helps maintain stable internal environmental conditions. Blood is composed of *formed elements* suspended in a fluid extracellular matrix called *blood plasma.* The formed elements include *red blood cells, white blood cells,* and cell fragments called *platelets* (fig. 5.21). Most blood cells form in red marrow within the hollow parts of certain long bones. Chapter 12 describes blood in detail. Table 5.5 lists the characteristics of the connective tissues.

### PRACTICE

13. Describe the general characteristics of cartilage.
14. Explain why injured bone heals more rapidly than injured cartilage.
15. What are the major components of blood?

## 5.4 | Types of Membranes

After discussing epithelial and connective tissues, membranes are better understood. **Epithelial membranes** are thin, sheetlike structures composed of epithelium and underlying connective tissue, covering body surfaces and lining body cavities. The three major types of epithelial membranes are *serous, mucous,* and *cutaneous.*

**Serous** (se′rus) **membranes** line body cavities that lack openings to the outside. These membranes form the inner linings of the thorax (parietal pleura) and abdomen (parietal peritoneum), and they cover the organs in these cavities (visceral pleura and visceral peritoneum, respectively, as shown in figs. 1.11 and 1.12, p. 20). A serous membrane consists of a layer of simple squamous epithelium and a thin layer of areolar connective tissue. The cells of a serous membrane secrete watery *serous fluid,* which lubricates membrane surfaces.

**Mucous** (mu′cus) **membranes** line cavities and tubes that open to the outside of the body, including the oral and nasal cavities and the tubes of the digestive, respiratory, urinary, and reproductive systems. A mucous membrane consists of epithelium overlying a layer of areolar connective tissue. Goblet cells within a mucous membrane secrete *mucus.*

Another epithelial membrane is the **cutaneous** (ku-ta′ne-us) **membrane,** more commonly called skin. It is described in detail in chapter 6.

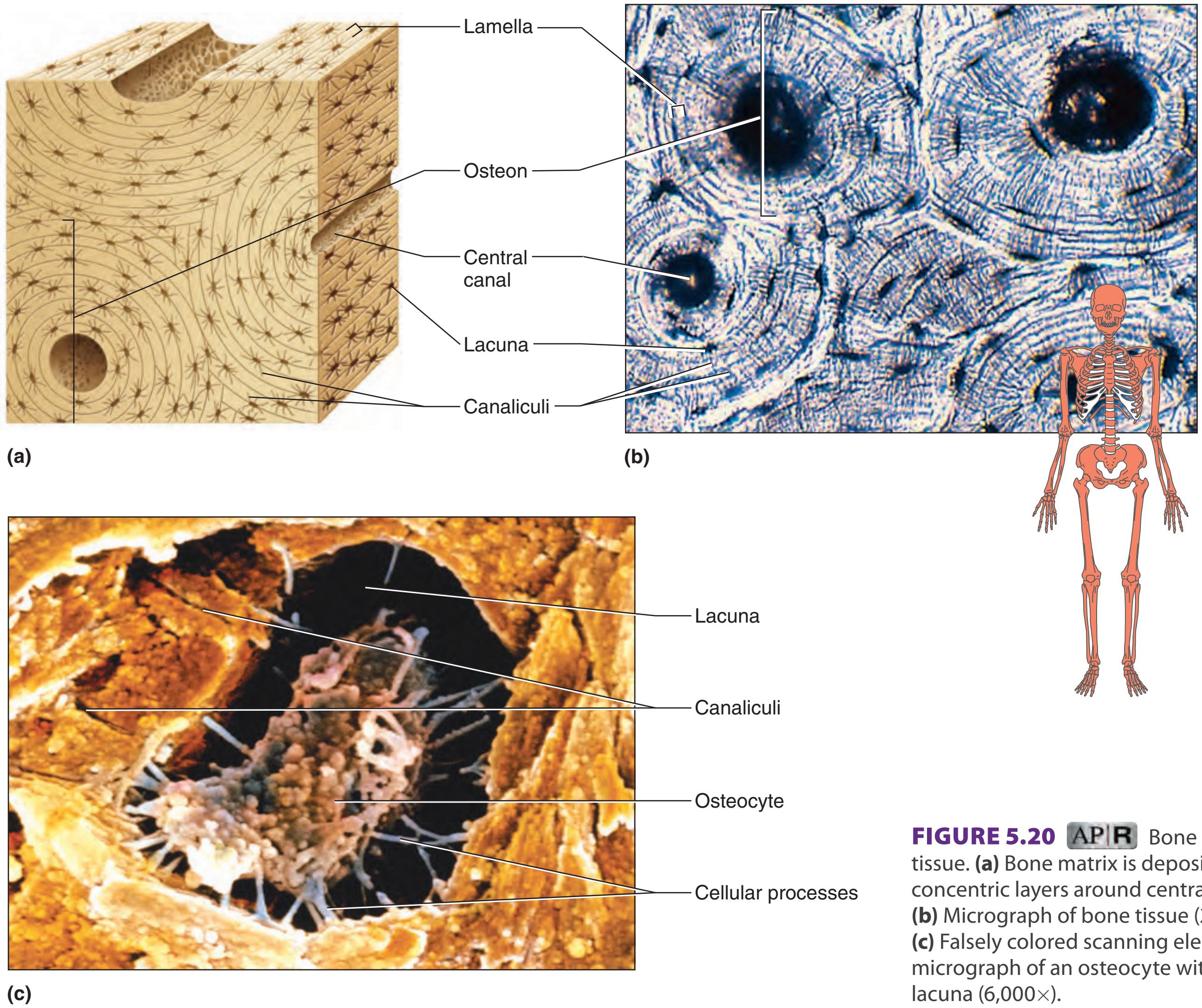


**FIGURE 5.20** APR Bone tissue. **(a)** Bone matrix is deposited in concentric layers around central canals. **(b)** Micrograph of bone tissue (200×). **(c)** Falsely colored scanning electron micrograph of an osteocyte within a lacuna (6,000×).

**TABLE 5.5 Connective Tissues**

| Type | Function | Location |
|---|---|---|
| Loose connective tissue | | |
| Areolar tissue | Binds organs | Beneath skin, between muscles, beneath epithelial tissues |
| Adipose tissue | Protects, insulates, stores fat | Beneath skin, around kidneys, behind eyeballs, on surface of heart |
| Reticular connective tissue | Supports | Walls of liver and spleen |
| Dense connective tissue | Binds organs | Tendons, ligaments, deeper layers of skin |
| Specialized connective tissue | | |
| Hyaline cartilage | Supports, protects, provides framework | Ends of bones, nose, rings in the walls of respiratory passages |
| Elastic cartilage | Supports, protects, provides flexible framework | Framework of external ear and parts of larynx |
| Fibrocartilage | Supports, protects, absorbs shock | Between bony parts of spinal column, parts of pelvic girdle and knee |
| Bone | Supports, protects, provides framework | Bones of skeleton |
| Blood | Transports substances, helps maintain stable internal environment | Throughout body within a closed system of blood vessels and heart chambers |

A different type of membrane, composed entirely of connective tissues, is a **synovial** (si-nove-al) **membrane.** It lines joints and is discussed further in chapter 7 (p. 174).

### PRACTICE

16. Name the four types of membranes, and explain how they differ.

## 5.5 | Muscle Tissues

### General Characteristics

**Muscle** (mus′el) **tissues** are able to contract. Their elongated cells, also called *muscle fibers,* can shorten and thicken. As they contract, muscle fibers pull at their attached ends, which moves body parts.

Approximately 40% of the body is skeletal muscle, and almost another 10% is smooth muscle or cardiac muscle. The three types of muscle tissue—skeletal, smooth, and cardiac—are introduced here and discussed in more detail in chapter 8.

### Skeletal Muscle Tissue

**Skeletal muscle tissue** forms muscles that usually attach to bones and can be controlled by conscious effort. For this reason, it is often called *voluntary* muscle tissue. The long, threadlike cells of skeletal muscle have alternating light and dark cross-markings called *striations.* Each cell has many nuclei (fig. 5.22). A nerve cell must stimulate a skeletal muscle cell to contract, and then the muscle cell relaxes when stimulation stops.

The muscles built of skeletal muscle tissue move the head, trunk, and limbs. They enable us to make facial expressions, write, talk, sing, chew, swallow, and breathe.

### Smooth Muscle Tissue

**Smooth muscle tissue** is so called because its cells do not have striations. Smooth muscle cells are shorter than skeletal muscle cells and are spindle-shaped, each with a single, centrally located nucleus (fig. 5.23). This tissue composes the walls of hollow internal organs, such as the stomach, intestine, urinary bladder, uterus, and blood vessels. Unlike skeletal muscle, smooth muscle cannot be stimulated to contract by conscious efforts. Thus, its actions are *involuntary.* For example, smooth muscle tissue moves food through the digestive tract, constricts blood vessels, and empties the urinary bladder.

### Cardiac Muscle Tissue

**Cardiac muscle tissue** is only in the heart. Its cells, which are striated and branched, are joined end to end, forming complex networks. Each cardiac muscle cell has a single nucleus (fig. 5.24). Where one cell touches another cell is a specialized intercellular junction called an *intercalated disc,* discussed further in chapter 8, p. 202.

Cardiac muscle, like smooth muscle, is controlled involuntarily. This tissue makes up the bulk of the heart and pumps blood through the heart chambers and into blood vessels.

### PRACTICE

17. List the general characteristics of muscle tissues.
18. Distinguish among skeletal, smooth, and cardiac muscle tissues.

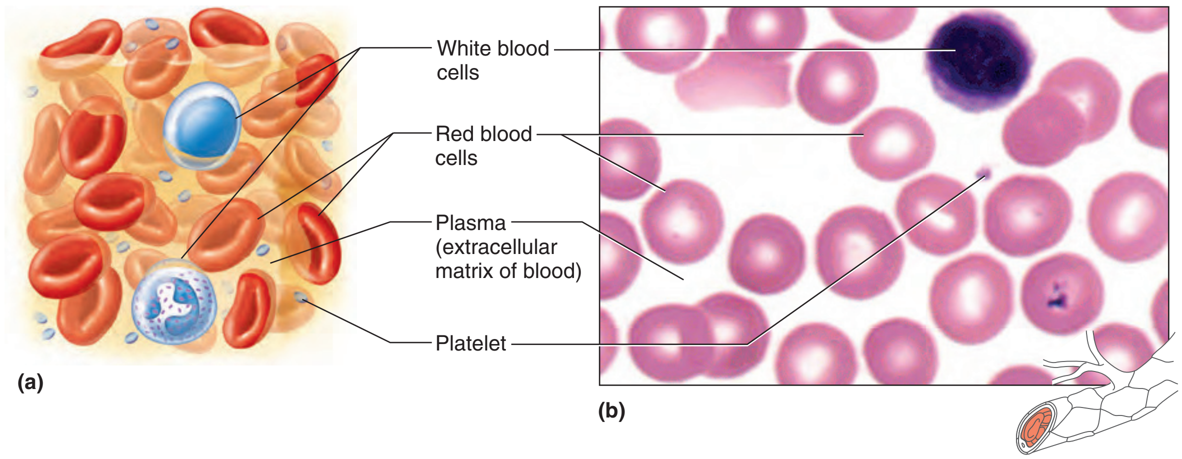


**FIGURE 5.21** Blood tissue consists of red blood cells, white blood cells, and platelets suspended in plasma (1,000×).

*What is the consistency of the extracellular matrix of this tissue?*
**Answer can be found in Appendix F on page 582.**

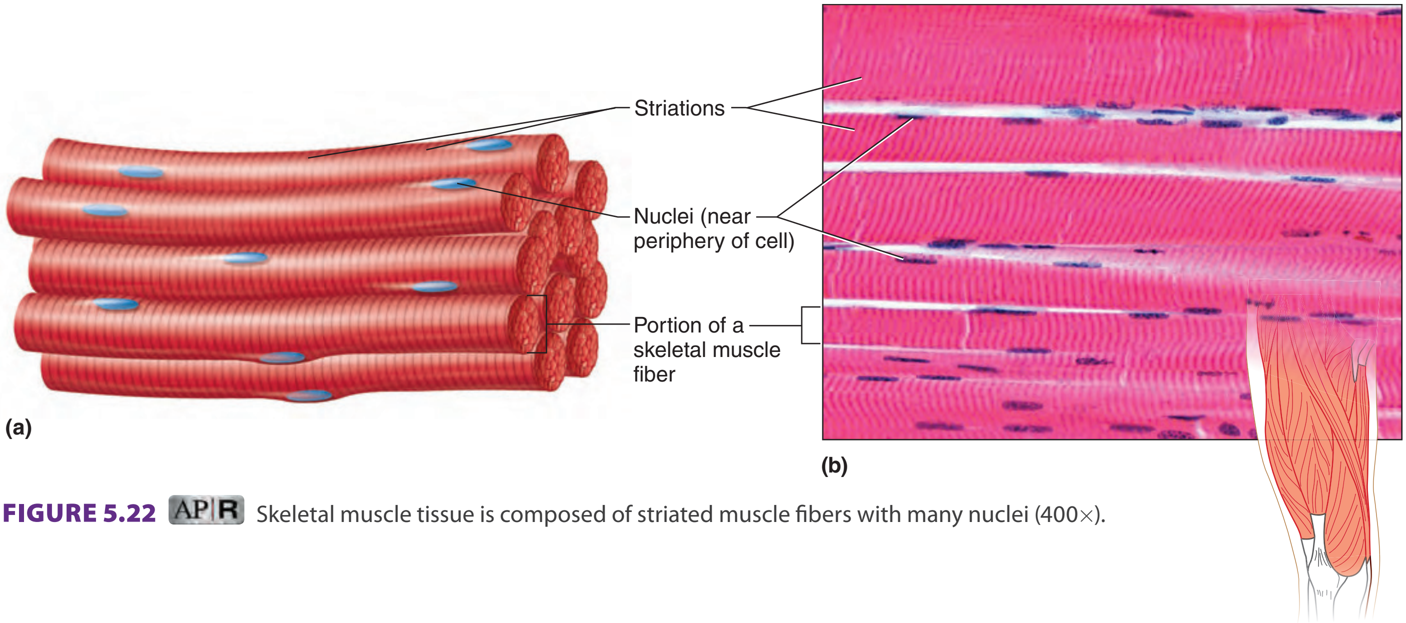

Striations
Nuclei (near periphery of cell)
Portion of a skeletal muscle fiber
(a)
(b)

**FIGURE 5.22** Skeletal muscle tissue is composed of striated muscle fibers with many nuclei (400×).

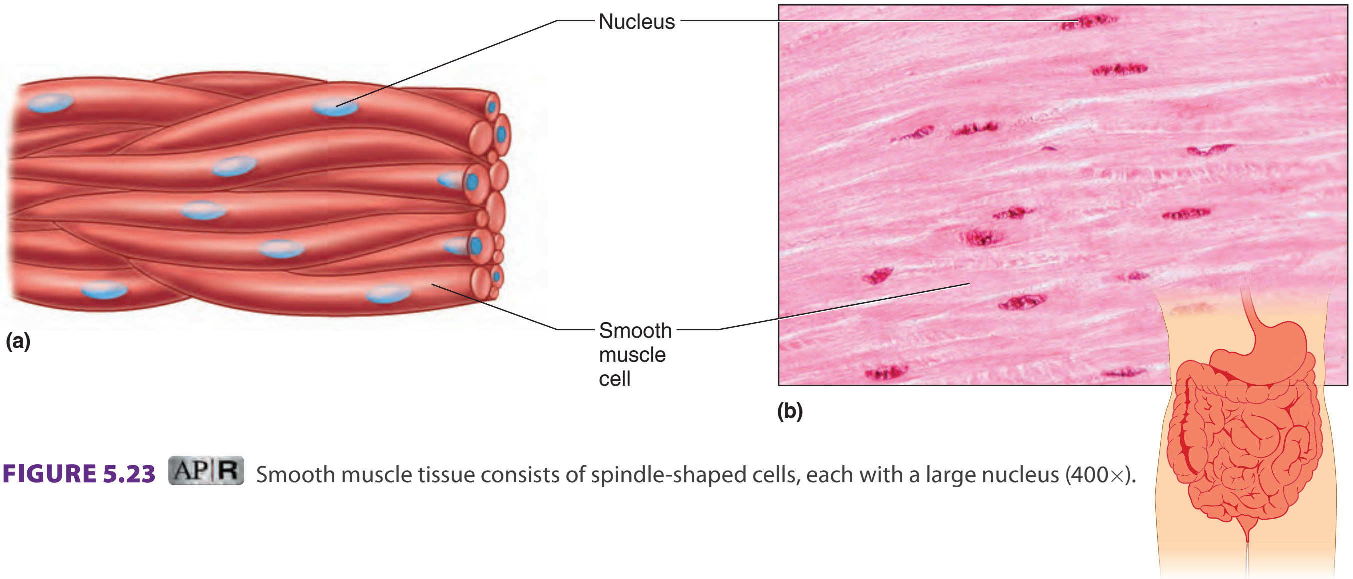


**FIGURE 5.23** Smooth muscle tissue consists of spindle-shaped cells, each with a large nucleus (400×).

## 5.6 | Nervous Tissues

**Nervous** (ner′vus) **tissues** are found in the brain, spinal cord, and peripheral nerves. The basic cells are called **neurons** (nu′ronz), or nerve cells (fig. 5.25). Neurons sense certain types of changes in their surroundings. They respond by conducting electrical impulses along cellular processes called *axons*. As a result of the patterns by which neurons communicate with each other and with muscle and gland cells, they can coordinate, regulate, and integrate many body functions.

In addition to neurons, nervous tissue includes **neuroglia** (nu-ro′gle-ah), shown in figure 5.25. Neuroglia divide and are crucial to the functioning of neurons. These cells support and bind the components of nervous tissue, carry on phagocytosis, and help supply growth factors and nutrients to neurons by connecting them to blood vessels. They also play a role in cell-to-cell communication. Nervous tissue is discussed in more detail in chapter 9. Table 5.6 summarizes the general characteristics of muscle and nervous tissues.

**PRACTICE**

19. Describe the general characteristics of nervous tissues.
20. Distinguish between neurons and neuroglia.

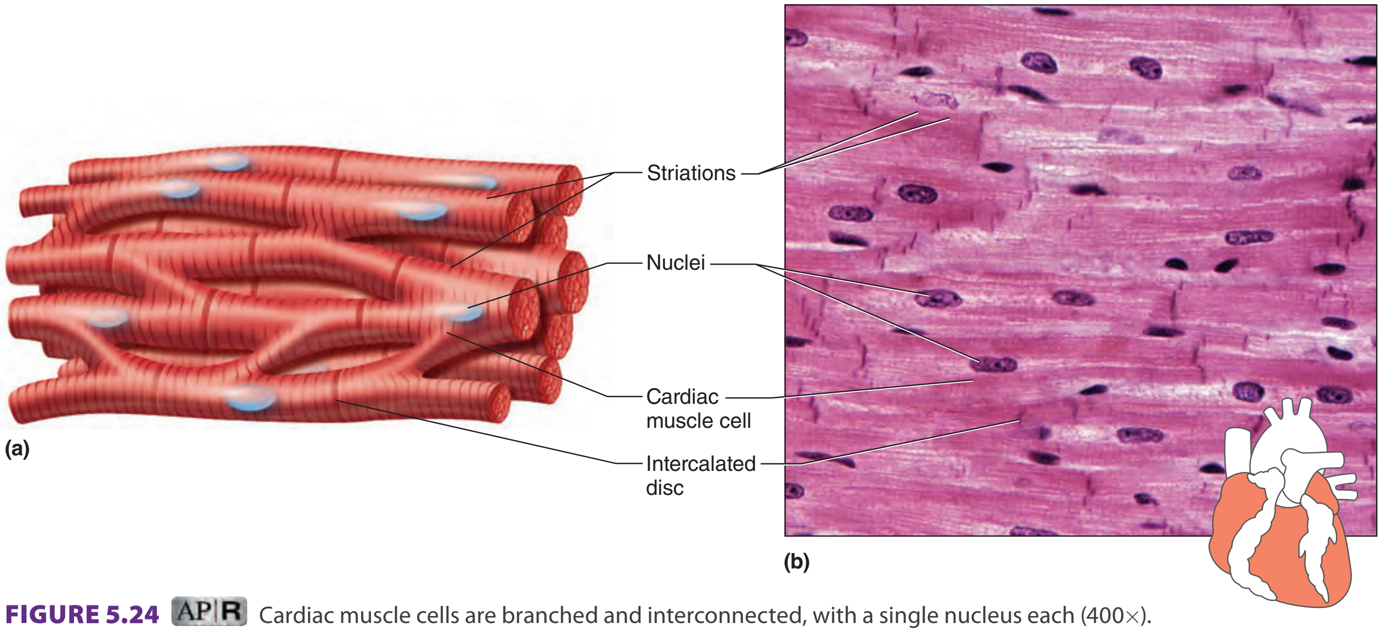


**FIGURE 5.24** APIR Cardiac muscle cells are branched and interconnected, with a single nucleus each (400×).

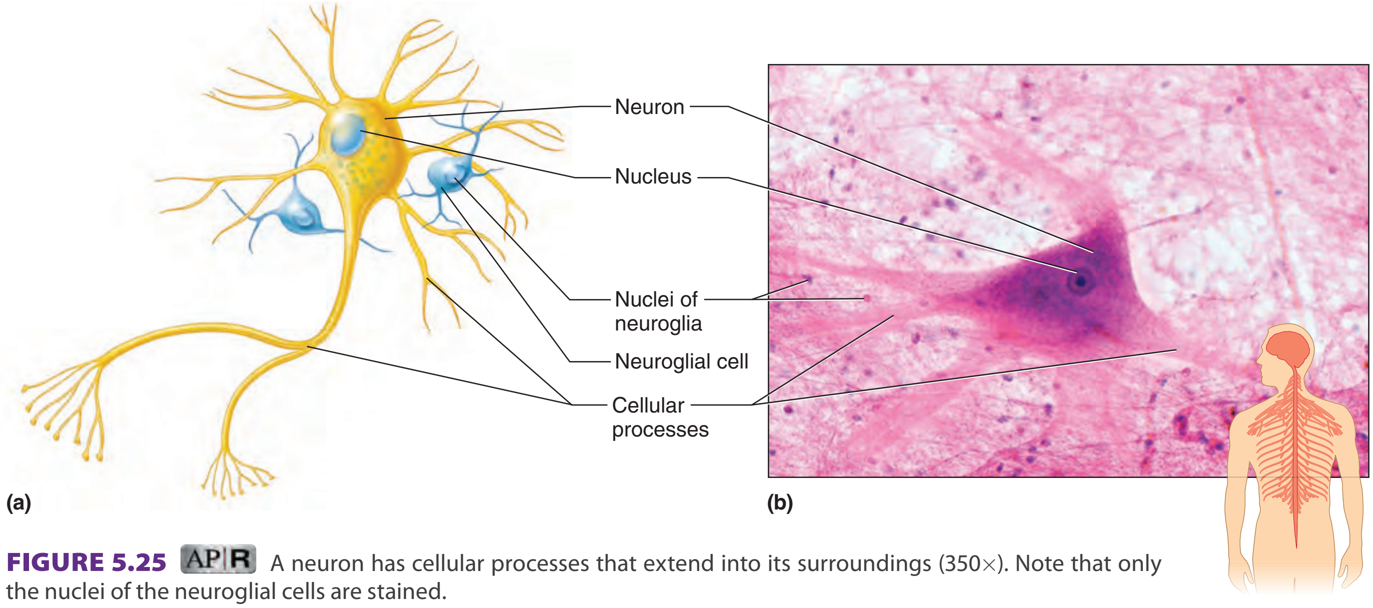


**FIGURE 5.25** APIR A neuron has cellular processes that extend into its surroundings (350×). Note that only the nuclei of the neuroglial cells are stained.

The cells of different tissues vary greatly in their abilities to divide. Cells that divide continuously include the epithelial cells of the skin and the inner lining of the digestive tract, and the connective tissue cells that form blood cells in red bone marrow. However, skeletal and cardiac muscle cells and nerve cells do not usually divide at all after differentiating.

Fibroblasts respond rapidly to injuries by increasing in number and fiber production. They help to repair tissues that have limited abilities to regenerate. For instance, fibroblasts form scar tissue where a heart attack occurs. Many organs include pockets of stem or progenitor cells that can divide and replace damaged, differentiated cells, under certain conditions.

**TABLE 5.6 Muscle and Nervous Tissues**

| Type | Function | Location |
|---|---|---|
| Skeletal muscle tissue (striated) | Voluntary movements of skeletal parts | Muscles usually attached to bones |
| Smooth muscle tissue (lacks striations) | Involuntary movements of internal organs | Walls of hollow internal organs |
| Cardiac muscle tissue (striated) | Heart movements | Heart muscle |
| Nervous tissue | Sensory reception and conduction of electrical impulses | Brain, spinal cord, and peripheral nerves |

# Summary Outline

## 5.1 Introduction (p. 105)

*Tissues are groups of cells with specialized structural and functional roles. The four major types of human tissue are epithelial, connective, muscle, and nervous.*

## 5.2 Epithelial Tissues (p. 105)

1. General characteristics
   - a. Epithelial tissue covers organs, lines cavities and hollow organs, and is the major tissue of glands.
   - b. Epithelium is anchored to connective tissue by a basement membrane, lacks blood vessels, consists of tightly packed cells, and is replaced continuously.
   - c. It functions in protection, secretion, absorption, and excretion.
   - d. Epithelial tissues are classified according to cell shape and number of cell layers.
2. Simple squamous epithelium
   - a. This tissue consists of a single layer of thin, flattened cells.
   - b. It functions in gas exchange in the lungs and lines blood and lymph vessels and is part of the membranes lining body cavities and covering viscera.
3. Simple cuboidal epithelium
   - a. This tissue consists of a single layer of cube-shaped cells.
   - b. It carries on secretion and absorption in the kidneys and various glands.
4. Simple columnar epithelium
   - a. This tissue is composed of elongated cells whose nuclei are near the basement membrane.
   - b. It lines the uterus and digestive tract.
   - c. Many absorbing cells have microvilli.
   - d. This tissue has goblet cells that secrete mucus.
5. Pseudostratified columnar epithelium
   - a. Nuclei located at two or more levels give this tissue a stratified appearance.
   - b. Cilia that are part of this tissue move mucus over the surface of the tissue.
   - c. It lines respiratory passages.
6. Stratified squamous epithelium
   - a. This tissue is composed of many layers of cells.
   - b. It protects underlying cells.
   - c. It forms the outer layer of the skin and lines the oral cavity, esophagus, vagina, and anal canal.
7. Stratified cuboidal epithelium
   - a. This tissue is composed of two or three layers of cube-shaped cells.
   - b. It lines the ducts of the mammary glands, sweat glands, salivary glands, and pancreas.
   - c. It protects.
8. Stratified columnar epithelium
   - a. The top layer of cells in this tissue are column-shaped. Cube-shaped cells make up the bottom layers.
   - b. It is in part of the male urethra and the lining of the larger ducts of exocrine glands.
   - c. This tissue protects and secretes.
9. Transitional epithelium
   - a. This tissue is specialized to stretch.
   - b. It lines the urinary bladder, ureters, and superior urethra.
10. Glandular epithelium
    - a. Glandular epithelium is composed of cells that are specialized to secrete substances.
    - b. A gland consists of one or more cells.
      - (1) Exocrine glands secrete into ducts.
      - (2) Endocrine glands secrete into tissue fluid or blood.
    - c. Exocrine glands are classified according to the composition of their secretions.
      - (1) Merocrine glands secrete fluid without loss of cytoplasm.
        - (a) Serous cells secrete watery fluid with a high enzyme content.
        - (b) Mucous cells secrete mucus.
      - (2) Apocrine glands lose portions of their cells during secretion.
      - (3) Holocrine glands release cells filled with secretory products.

## 5.3 Connective Tissues (p. 113)

1. General characteristics
   - a. Connective tissue connects, supports, protects, provides frameworks, fills spaces, stores fat, produces blood cells, protects against infection, and helps repair damaged tissues.
   - b. Connective tissue cells usually have considerable extracellular matrix between them.
   - c. This extracellular matrix consists of fibers and ground substance.
   - d. Major cell types
     - (1) Fibroblasts produce collagen and elastic fibers.
     - (2) Macrophages are phagocytes.
     - (3) Mast cells may release heparin and histamine, and usually are near blood vessels.
   - e. Connective tissue fibers
     - (1) Collagen fibers have great tensile strength.
     - (2) Elastic fibers are composed of elastin and are very elastic.
     - (3) Reticular fibers are thin collagen fibers.
2. Categories of connective tissue
   Connective tissue proper includes loose connective tissue and dense connective tissue. Specialized connective tissue includes cartilage, bone, and blood.
   - a. Loose connective tissue
     - (1) Areolar tissue forms thin membranes between organs and binds them. It is beneath the skin and between muscles.
     - (2) Adipose tissue stores fat, cushions, and insulates. It is found beneath the skin, in certain abdominal membranes, behind the eyeballs, and around the kidneys, heart, and various joints.
     - (3) Reticular connective tissue is composed of thin, collagen fibers. It helps provide the framework of the liver and spleen.
   - b. Dense connective tissue
     - (1) This tissue is largely composed of strong, collagen fibers.
     - (2) It is found in the tendons, ligaments, white portions of the eyes, and the deeper skin layer.
   - c. Cartilage
     - (1) Cartilage provides a supportive framework for various structures.
     - (2) Its extracellular matrix is composed of fibers and a gel-like ground substance.
     - (3) Cartilaginous structures are enclosed in a perichondrium, which contains blood vessels.
     - (4) Cartilage lacks a direct blood supply and is slow to heal.
     - (5) Major types are hyaline cartilage, elastic cartilage, and fibrocartilage.
   - d. Bone
     - (1) The extracellular matrix of bone contains mineral salts and collagen.
     - (2) Its cells are usually organized in concentric circles around central canals. Canaliculi connect the cells.
     - (3) Bone is an active tissue that heals rapidly.

   e. Blood
      (1) Blood transports substances and helps maintain a stable internal environment.
      (2) Blood is composed of red blood cells, white blood cells, and platelets suspended in plasma.
      (3) Blood cells develop in red marrow in the hollow parts of long bones.

### 5.4 Types of Membranes (p. 119)

1. Epithelial membranes are composed of epithelium and underlying connective tissue. Serous, mucous, and cutaneous membranes are epithelial membranes.
2. Serous membranes, composed of epithelium and areolar connective tissue, are membranes that line body cavities lacking openings to the outside and cover the organs in these cavities. The cells of a serous membrane secrete serous fluid to lubricate membrane surfaces.
3. Mucous membranes, composed of epithelium and areolar connective tissue, are membranes that line body cavities opening to the outside. Goblet cells within these membranes secrete mucus.
4. Another epithelial membrane, the cutaneous membrane, is the external body covering commonly called skin.
5. Synovial membranes, composed entirely of connective tissues, line joints.

### 5.5 Muscle Tissues (p. 121)

1. General characteristics
   a. Muscle cells are also called muscle fibers.
   b. Muscle tissues contract, moving structures that are attached to them.
   c. The three types are skeletal, smooth, and cardiac muscle tissues.
2. Skeletal muscle tissue
   a. Muscles containing this tissue usually are attached to bones and controlled by conscious effort.
   b. Cells are long and threadlike, with many nuclei and striations.
   c. Muscle cells contract when stimulated by nerve cells, and then relax when stimulation stops.
3. Smooth muscle tissue
   a. This tissue is in the walls of hollow internal organs.
   b. It is involuntarily controlled.
4. Cardiac muscle tissue
   a. This tissue is found only in the heart.
   b. Cells are joined by intercalated discs and form branched networks.

### 5.6 Nervous Tissues (p. 122)

1. Nervous tissues are in the brain, spinal cord, and peripheral nerves.
2. Neurons (nerve cells)
   a. Neurons sense changes and respond by conducting electrical impulses to other neurons or to muscles or glands.
   b. They coordinate, regulate, and integrate body activities.
3. Neuroglia
   a. Some of these cells bind and support nervous tissue.
   b. Others carry on phagocytosis.
   c. Still others connect neurons to blood vessels.
   d. Some are involved in cell-to-cell communication.

## CHAPTER ASSESSMENTS

### 5.1 Introduction

**1.** Which of the following is a major tissue type in the body? (p. 105)
   a. epithelial
   b. connective
   c. muscle
   d. all of the above

**2.** Which is the type of tissue that functions in secretion and absorption? (p. 105)
   a. epithelial
   b. connective
   c. muscle
   d. nervous

### 5.2 Epithelial Tissues

**3.** A general characteristic of epithelial tissues is that ______. (p. 105)
   a. numerous blood vessels are present
   b. cells are spaced apart
   c. cells readily divide
   d. there is much extracellular matrix between cells

**4.** Explain how the structure of epithelial tissues provides for the functions of epithelial tissues. (p. 106)

**5.** Match the epithelial tissue to an organ in which the tissue is found. (pp. 106–111)
   (1) simple squamous epithelium
   (2) simple cuboidal epithelium
   (3) simple columnar epithelium
   (4) pseudostratified columnar epithelium
   (5) stratified squamous epithelium
   (6) stratified cuboidal epithelium
   (7) stratified columnar epithelium
   (8) transitional epithelium
   (9) glandular epithelium

   A. lining of intestines
   B. lining of ducts of mammary glands
   C. lining of urinary bladder
   D. salivary glands
   E. air sacs of lungs
   F. respiratory passages
   G. parts of male urethra
   H. lining of kidney tubules
   I. outer layer of skin

**6.** Distinguish between exocrine and endocrine glands. (p. 111)

**7.** A gland that secretes substances out of cells by exocytosis is a(n) ______________. (p. 111)
   a. merocrine gland
   b. apocrine gland
   c. holocrine gland
   d. mammary gland

### 5.3 Connective Tissues

**8.** Define *extracellular matrix.* (p. 113)

**9.** Describe three major types of connective tissue cells. (p. 113)

**10.** Distinguish between collagen and elastin. (p. 115)

**11.** Compare and contrast the different types of loose connective tissue. (p. 116)

**12.** Describe dense connective tissue. (p. 116)

**13.** Explain why injured dense connective tissue and cartilage are usually slow to heal. (p. 117)

**14.** Name the types of cartilages and describe their differences and similarities. (p. 118)

**15.** Describe how bone cells are organized in bone tissue. (pp. 118–119)

**16.** The fluid extracellular matrix of blood is called ________. (p. 119)
   a. white blood cells
   b. red blood cells
   c. platelets
   d. plasma

### 5.4 Types of Membranes

**17.** Identify the locations of four types of membranes in the body and indicate the types of tissues making up each membrane. (pp. 119–121)

### 5.5 Muscle Tissues

**18.** Compare and contrast skeletal, smooth, and cardiac muscle tissues in terms of location, cell appearance, and control. (p. 121)

### 5.6 Nervous Tissues

**19.** Distinguish between the functions of neurons and neuroglia. (p. 122)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 3.2, 3.4, 5.1, 5.2, 5.3, 5.5, 5.6

1. Tissue engineering combines living cells with synthetic materials to create functional substitutes for human tissues. What components would you use to engineer replacement (a) skin, (b) bone, (c) muscle, and (d) blood?
2. Cancer-causing agents (carcinogens) usually act on dividing cells. Which of the four major types of tissues would carcinogens most influence? Least influence?

### OUTCOMES 5.2, 5.4

3. Sometimes, in response to irritants, mucous cells secrete excess mucus. What symptoms might this produce if it occurred in the (a) digestive tract or (b) respiratory tract?

### OUTCOME 5.3

4. Collagen and elastin are added to many beauty products. What type of tissues are they normally part of?
5. Joints such as the elbow, shoulder, and knee contain considerable amounts of cartilage and dense connective tissue. How does this explain why joint injuries are often slow to heal?
6. Disorders of collagen are characterized by deterioration of connective tissues. Why would you expect such diseases to produce widely varying symptoms?

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# 6

# Integumentary System

*Eczema on a person's elbow.*

**A** skin protein that raises allergy risk. What do the dry itchy skin of atopic dermatitis, the itchy red skin of eczema, the sneezing and runny eyes of hay fever, and the contracting airways of asthma share? A deficiency of a skin protein called filaggrin sets the stage for developing allergies ("false alarm" immune reactions against dangerous substances).

Researchers had wondered why people who suffered from atopic dermatitis as children often develop food allergies, asthma, hay fever, and susceptibility to herpes infections as adults. Filaggrin may explain the link between skin conditions and allergies.

Filaggrin is a large protein that binds to the keratin proteins that fill the scaly cells that make up the outermost layer of the skin, the epidermis. In healthy skin, filaggrin is broken down, releasing amino acids that rise to the surface of the skin and block water from leaving the skin, keeping the skin moist. The wetness and the tight packing of the epidermal cells keep out irritants, disease-causing organisms, and substances that trigger allergic reactions.

People with the rare inherited form of the disease ichthyosis vulgaris, which causes severe skin flaking, have two mutations in the gene that encodes filaggrin. As many as one in ten of us have a mutation in the filaggrin gene that causes mild ichthyosis, treatable with skin lotion.

When researchers realized that people with either form of ichthyosis very often also develop the allergic condition eczema, they hypothesized that filaggrin could be the link. When the epidermis is dry and cracked due to deficient filaggrin, allergens can enter and reach deeper skin layers, where they encounter and activate immune system cells, which signal inflammation. Eczema results. Later, inhaling the same allergens that once crossed the broken skin provokes an immune response in the airways, causing asthma. Experiments are testing treatments of breaks in the skin early in life that might prevent eczema, asthma, and other allergies later in life.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 6.1 Introduction

1. Describe what constitutes an organ, and name the large organ of the integumentary system. (p. 128)

### 6.2 Skin and Its Tissues

2. List the general functions of the skin. (p. 128)
3. Describe the structure of the layers of the skin. (p. 128)
4. Summarize the factors that determine skin color. (p. 130)

### 6.3 Accessory Structures of the Skin

5. Describe the accessory structures associated with the skin. (pp. 133–135)

### 6.4 Regulation of Body Temperature

6. Explain how the skin helps regulate body temperature. (p. 136)

### 6.5 Healing of Wounds

7. Describe wound healing. (p. 136)

**Module 4:** Integumentary System

## AIDS TO UNDERSTANDING WORDS *(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**cut-** [skin] sub*cut*aneous: Beneath the skin.
**derm-** [skin] *derm*is: Inner layer of the skin.
**epi-** [upon] *epi*dermis: Outer layer of the skin.
**follic-** [small bag] hair *follic*le: Tubelike depression in which a hair develops.
**kerat-** [horn] *kerat*in: Protein produced as epidermal cells die and harden.
**melan-** [black] *melan*in: Dark pigment produced by certain cells.
**seb-** [grease] *seb*aceous gland: Gland that secretes an oily substance.
**sudor-** [sweat] *sudor*iferous glands: Exocrine glands that secrete sweat.

## 6.1 | Introduction

Two or more types of tissues grouped together and performing specialized functions constitute an **organ** (see fig. 1.3, p. 12). The skin is the largest organ in the body by weight. Skin and its accessory structures (hair, nails, sensory receptors, and glands) make up the **integumentary** (in-teg-u-men′tar-e) **system.** The skin forms a barrier between ourselves and the outside, and is a strong yet flexible covering for our bodies.

**FACTS OF LIFE** If the skin of a 150-pound person were spread out flat, it would cover approximately 20 square feet.

**PRACTICE**

1. What constitutes an organ?

## 6.2 | Skin and Its Tissues

The skin is one of the most versatile organs of the body. It is vital in maintaining homeostasis. In addition to providing a protective covering, the skin helps regulate body temperature, retards water loss from deeper tissues, houses sensory receptors, synthesizes various biochemicals, and excretes small amounts of wastes.

The skin plays a role in the production of vitamin D, which is necessary for normal bone and tooth development. This vitamin can be obtained in the diet or can form from a substance (dehydrocholesterol) that is synthesized by cells in the digestive system. When dehydrocholesterol reaches the skin by means of the blood and is exposed to ultraviolet light from the sun, it changes to vitamin D in an inactive form (cholecalciferol). In the liver and kidneys the inactive form is modified and becomes active vitamin D (calcitriol).

The skin includes two distinct layers (fig. 6.1). The outer layer, called the **epidermis** (ep″ĭ-der′mis), is composed of stratified squamous epithelium. The inner layer, or **dermis** (der′mis), is thicker than the epidermis. It includes connective tissue consisting of collagen and elastic fibers, epithelial tissue, smooth muscle tissue, nervous tissue, and blood. A *basement membrane* anchors the epidermis to the dermis and separates these two skin layers.

Various treatments temporarily smooth facial wrinkles. "Botox" is an injection of a very dilute solution of botulinum toxin. Produced by the bacterium *Clostridium botulinum,* the toxin causes food poisoning. It also blocks nerve cell activation of the facial muscles that control smiling, frowning, and squinting. After three months, though, the facial nerve cells contact the muscles at different points, and the wrinkles return. (Botox used at higher doses to treat neuromuscular conditions can cause adverse effects.) Other anti-wrinkle treatments include chemical peels and dermabrasion to reveal new skin surface; collagen injections; and transplants of subcutaneous fat from the buttocks to the face.

Beneath the dermis are masses of areolar tissue and adipose tissue that bind the skin to the underlying organs, forming the **subcutaneous** (sub″ku-ta′ne-us) **layer** (hypodermis). As its name indicates, this layer is beneath the skin and not a true layer of the skin. The collagen and elastic fibers of this layer are continuous with those of the dermis. Most of these fibers run parallel to the surface of the skin, extending in all directions. As a result, no sharp boundary separates the dermis and the subcutaneous layer. The adipose tissue of the subcutaneous layer insulates, helping to conserve body heat. The subcutaneous layer also contains the major blood vessels that supply the skin and underlying adipose tissue.

**PRACTICE**

2. List the functions of the skin.
3. Name the tissues in the outer and inner layers of the skin.
4. Name the tissues in the subcutaneous layer beneath the skin.
5. What are the functions of the subcutaneous layer?

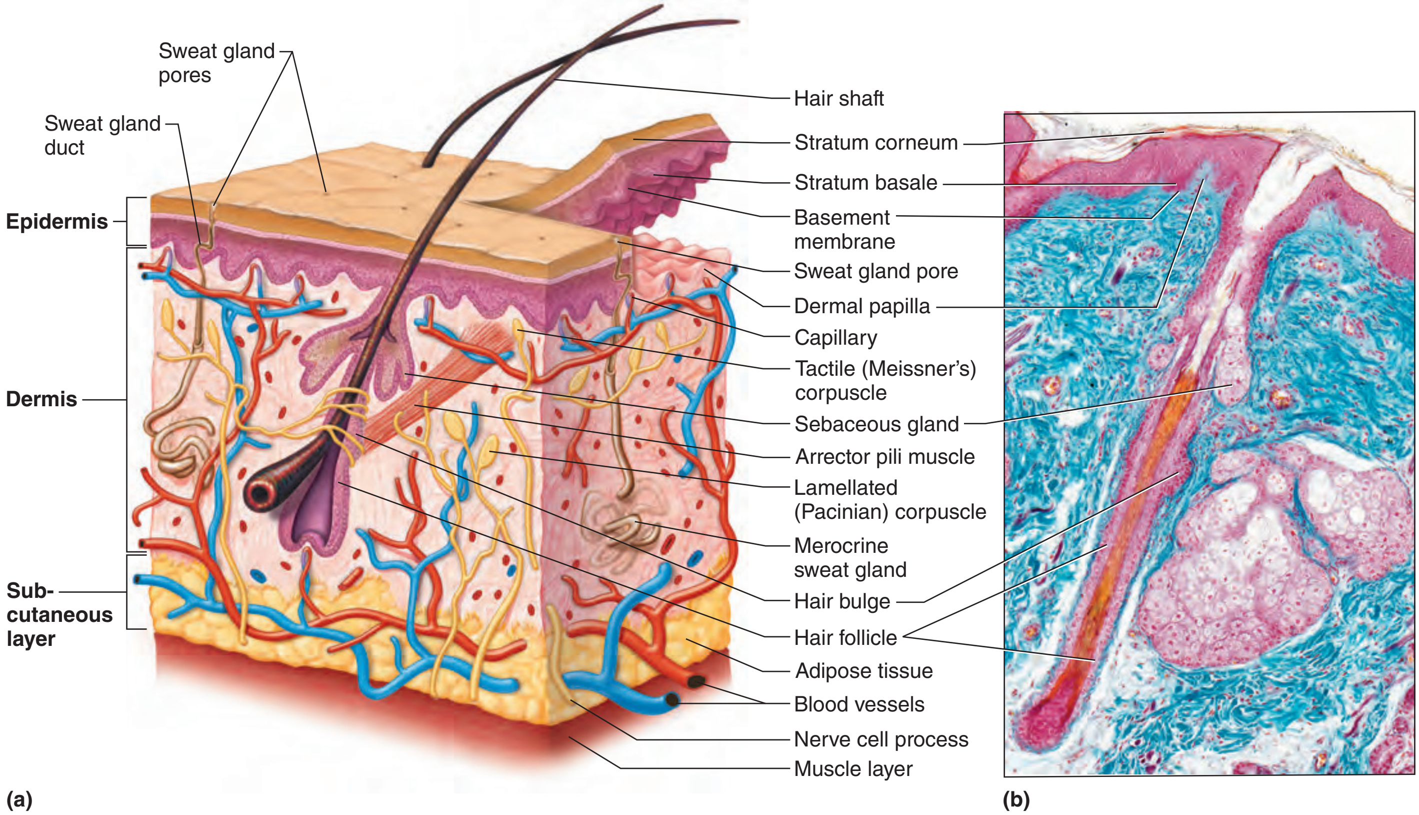

Sweat gland pores
Sweat gland duct
Epidermis
Dermis
Sub-cutaneous layer
Hair shaft
Stratum corneum
Stratum basale
Basement membrane
Sweat gland pore
Dermal papilla
Capillary
Tactile (Meissner's) corpuscle
Sebaceous gland
Arrector pili muscle
Lamellated (Pacinian) corpuscle
Merocrine sweat gland
Hair bulge
Hair follicle
Adipose tissue
Blood vessels
Nerve cell process
Muscle layer
(a)
(b)

**FIGURE 6.1** APR Skin. **(a)** The skin is an organ that includes two layers, the epidermis and dermis, that lie atop a subcutaneous ("beneath the skin") layer. **(b)** This light micrograph depicts the layered structure of the skin (75×).

*Intradermal injections* are injected into the skin. *Subcutaneous injections* are administered through a hollow needle into the subcutaneous layer beneath the skin. Subcutaneous injections and *intramuscular injections,* administered into muscles, are sometimes called hypodermic injections.

Some substances are introduced through the skin by means of an adhesive transdermal patch that includes a small reservoir containing a drug. The drug passes from the reservoir through a permeable membrane at a known rate. It then diffuses into the epidermis and enters the blood vessels of the dermis. Transdermal patches deliver drugs that protect against motion sickness, alleviate chest pain associated with heart disease, and lower blood pressure. A transdermal patch that delivers nicotine is used to help people stop smoking.

## Epidermis

The epidermis lacks blood vessels because it is composed entirely of stratified squamous epithelium. However, the deepest layer of epidermal cells, called the *stratum basale* (stra′tum ba′sal), or stratum germinativum, is close to the dermis and is nourished by dermal blood vessels (fig. 6.1*a*). As the cells of this layer divide and grow, the older epidermal cells are pushed away from the dermis toward the skin surface. The farther the cells move, the poorer their nutrient supply becomes, and in time they die.

### CAREER CORNER

### Massage Therapist

The middle-aged woman feels something give way in her left knee as she lands from a jump in her dance class. She limps away between her much younger classmates, in great pain. At home, she uses "RICE"—rest, ice, compression, elevation—then has a friend take her to an urgent care clinic, where a physician diagnoses patellar tendinitis, or "jumper's knee." Frequent jumping followed by lateral movements caused the injury.

Three days later, at her weekly appointment with a massage therapist for stress relief, the woman mentions the injury. Over the next few weeks, the massage therapist applies light pressure to the injured area to stimulate circulation, and applies friction in a transverse pattern to break up scar tissue and relax the muscles. She also massages the muscles to improve flexibility.

A massage therapist manipulates soft tissues, using combinations of pressing, stroking, kneading, compressing, and vibrating, to relieve pain and reduce stress. Training includes 300 to 1,000 hours of class time, hands-on practice, and continuing education. Specialties include pediatrics, sports injuries, and even applying massage techniques to racehorses.

The older cells (keratinocytes) harden in a process called **keratinization** (ker″ah-tin″ĭ-za′shun). The cytoplasm fills with strands of tough, fibrous, waterproof *keratin* proteins. As a result, many layers of tough, tightly packed dead cells accumulate in the outermost layer of the epidermis, called the *stratum corneum* (kor′ne-um). These dead cells are eventually shed.

The thickness of the epidermis varies from region to region. In most areas, only four layers can be distinguished: the *stratum basale, stratum spinosum* (spi-no′sum), *stratum granulosum* (gran″u-lo′sum), and *stratum corneum.* An additional layer, the *stratum lucidum* (loo′sid-um), is in the thickened and hairless (glabrous) skin of the palms and soles (fig. 6.2). The stratum lucidum may be missing where the epidermis is thin over the rest of the body.

Healthy skin does not wear away completely because the production of epidermal cells is generally closely balanced with loss of dead cells from the stratum corneum. However, the rate of cell division increases where the skin is rubbed or pressed regularly, causing growth of thickened areas called *calluses* on the palms and soles, and keratinized conical masses on the toes called *corns.*

The epidermis has important protective functions. It shields the moist underlying tissues against excess water loss, mechanical injury, and the effects of harmful chemicals. Intact epidermis also keeps out disease-causing microorganisms (pathogens).

Specialized cells in the epidermis called *melanocytes* produce **melanin** (mel′ah-nin), a pigment that provides skin color (fig. 6.3*a*). Melanin also absorbs ultraviolet radiation in sunlight, which would otherwise cause mutations in the DNA of skin cells and other damaging effects. Melanocytes lie in the deepest portion of the epidermis. They are the only cells that can produce melanin, but the pigment may also appear in nearby epidermal cells. Melanocytes have long, pigment-containing cellular extensions that pass upward between neighboring epidermal cells (fig. 6.3*b*). These extensions transfer melanin granules into neighboring cells by a process called *cytocrine secretion,* providing the pigmentation. The neighboring epidermal cells may actually contain more melanin than the melanocytes (fig. 6.3*b*). Clinical Application 6.1 discusses skin cancer arising from melanocytes and other epidermal cells.

### *Skin Color*

Skin color is due largely to melanin. All people have about the same number of melanocytes in their skin. Differences in skin color result from differences in the amount of melanin that melanocytes produce and in the distribution and size of the pigment granules. Skin color is mostly genetically determined. If genes instruct melanocytes to produce abundant melanin, the skin is dark.

**FACTS OF LIFE** More than a hundred genes affect pigmentation of the skin, hair, and irises of the eyes.

Environmental and physiological factors also influence skin color. Sunlight, ultraviolet light from sun-

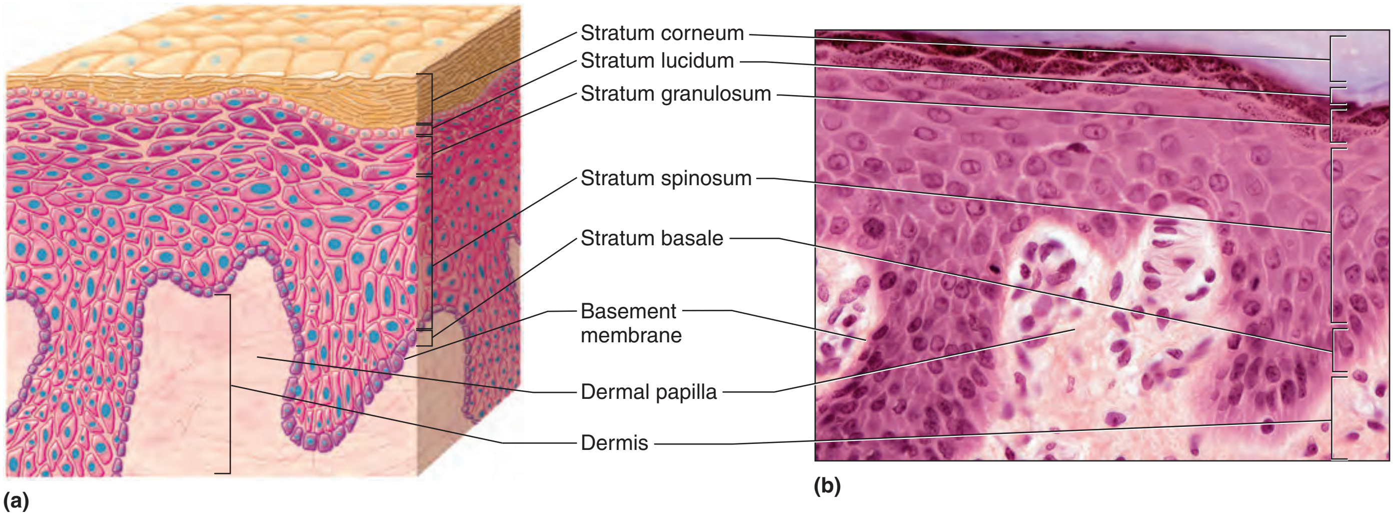
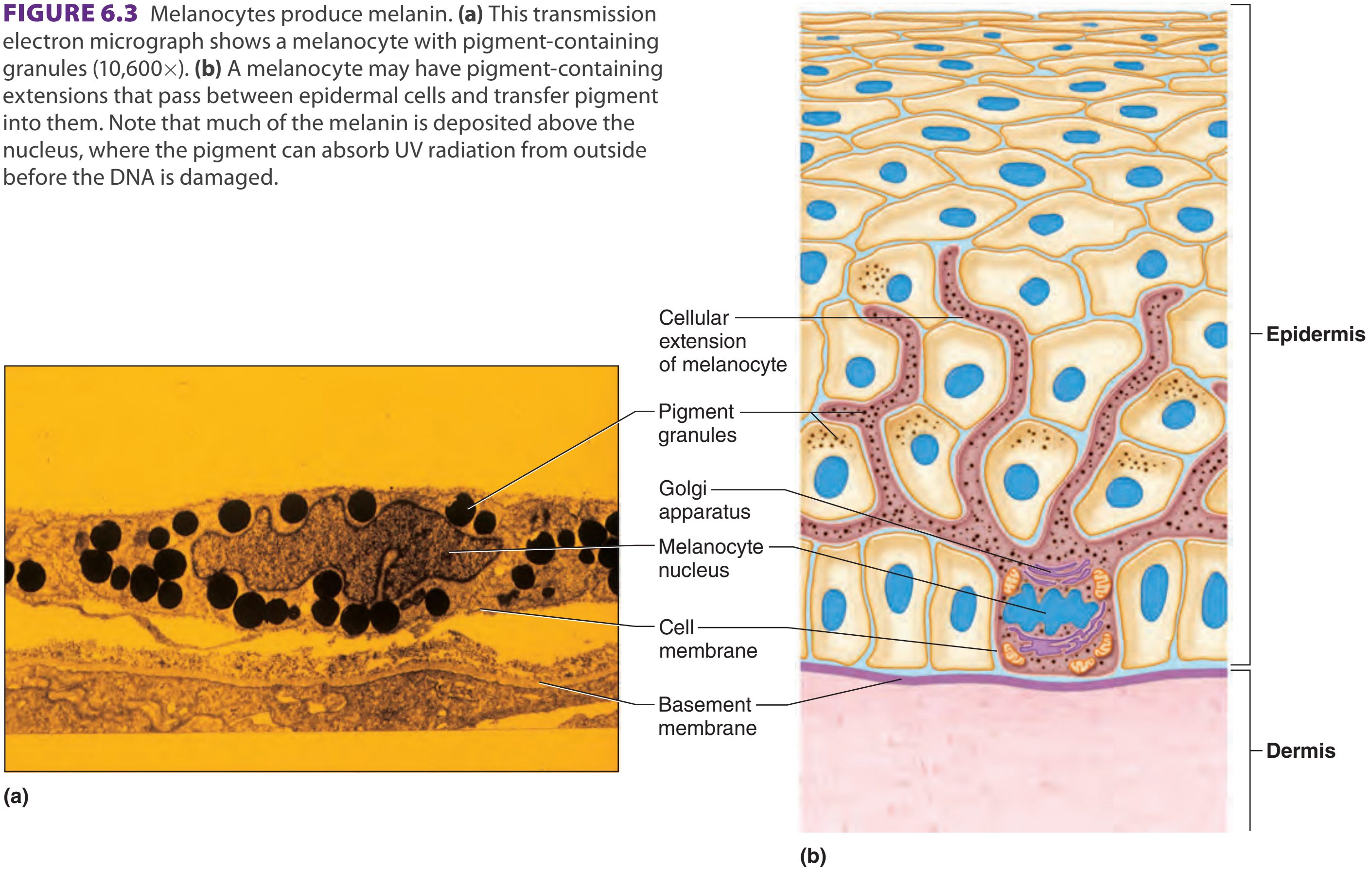


**FIGURE 6.2** APR Epidermis of thick skin. **(a)** The layers of the epidermis are distinguished by changes in cells as they are pushed toward the surface of the skin. **(b)** Light micrograph of skin (500×).

Q *Where is thick skin found on the body?*

**Answer can be found in Appendix F on page 582.**

**FIGURE 6.3** Melanocytes produce melanin. **(a)** This transmission electron micrograph shows a melanocyte with pigment-containing granules (10,600×). **(b)** A melanocyte may have pigment-containing extensions that pass between epidermal cells and transfer pigment into them. Note that much of the melanin is deposited above the nucleus, where the pigment can absorb UV radiation from outside before the DNA is damaged.



lamps, and X rays darken existing melanin and stimulate production of additional pigment. Blood in the dermal vessels may affect skin color as physiological changes occur. When blood is well oxygenated, the blood pigment (hemoglobin) is bright red, making the skin of light-complexioned people appear pinkish. When the blood oxygen concentration is low, hemoglobin is dark red, and the skin appears bluish—a condition called *cyanosis.* Other physiological factors affect skin color. For example, a diet high in yellow vegetables may turn skin orange-yellow, because these foods are rich in a pigment called carotene, which accumulates in the stratum corneum and adipose tissue of the dermis and subcutaneous layers. Skin color can also be affected by disease. A yellowish tone can indicate *jaundice*, which is a consequence of liver malfunction.

**PRACTICE**

6. Explain how the epidermis is formed.
7. Distinguish between the stratum basale and the stratum corneum.
8. What is the function of melanin?
9. Which factors influence skin color?

## Dermis

The boundary between the epidermis and dermis is uneven because epidermal ridges project inward and conical projections of dermis, called dermal papillae, extend into the spaces between the ridges (see fig. 6.1). Dermal papillae are found in the skin all over the body, but they are most abundant in the hands and feet. The friction ridges formed by the dermal papillae leave a patterned impression when a finger is pressed against a surface—a fingerprint. Genes determine general fingerprint patterns. Fingerprint patterns change slightly as a fetus presses the forming ridges against the uterine wall. No two fetuses move exactly in the same ways, so even the fingerprints of identical twins are not exactly alike.

The dermis binds the epidermis to underlying tissues (see fig. 6.1*a*). It is composed of areolar tissue along with dense connective tissue that includes tough collagen fibers and elastic fibers within a gel-like ground substance. Networks of these fibers give the skin toughness and elasticity.

Dermal blood vessels supply nutrients to all skin cells. These vessels also help regulate body temperature, as explained later in this chapter on page 136.

## CLINICAL APPLICATION 6.1

## Skin Cancer

Skin cancer arises in nonpigmented epithelial cells in the deep layer of the epidermis, or from melanocytes. Skin cancers originating from epithelial cells are called *cutaneous carcinomas* (squamous cell carcinoma and basal cell carcinoma); those arising from melanocytes are *cutaneous melanomas* (melanocarcinomas or malignant melanomas) (fig. 6A). Statistically, one in five people in the United States will develop skin cancer at some point.

Cutaneous carcinomas are the most common type of skin cancer, occurring mostly in light-skinned people over forty years of age regularly exposed to sunlight. Cutaneous carcinomas typically develop from hard, dry, scaly growths that have reddish bases. They may be flat or raised and usually firmly adhere to the skin. They are most common on the neck, face, or scalp. Cutaneous carcinomas grow slowly and are usually cured with surgical removal or radiation treatment.

Cutaneous melanomas are pigmented with melanin, often with a variety of colored areas, such as variegated brown, black, gray, or blue. Melanomas usually have irregular rather than smooth outlines, and may feel bumpy. The "ABCDE" rule provides a checklist for melanoma: A for asymmetry; B for border (irregular); C for color (more than one); D for diameter (more than 6 millimeters); and E for elevation.

People of any age may develop cutaneous melanomas. These cancers are caused by short, intermittent exposure to high-intensity sunlight, such as when a person who usually stays indoors occasionally sustains a blistering sunburn.

A cutaneous melanoma, usually appears on the back or limbs, arising from normal-appearing skin or from a mole (nevus). The lesion spreads horizontally through the skin, but may thicken and grow downward, invading deeper tissues. Surgical removal during the horizontal growth phase arrests the cancer in six of every seven cases. However, once it thickens and spreads into deeper tissues, it becomes difficult to treat, and the survival rate is low.

Both UVA and UVB types of ultraviolet radiation, which are different wavelengths of energy, can cause the mutations that trigger skin cancer. To reduce the risk of developing skin cancer, avoid exposing the skin to high-intensity sunlight, use sunscreens and sunblocks that reflect or repel UV wavelengths, and examine the skin regularly. Report any "ABCDE" lesions to a physician.

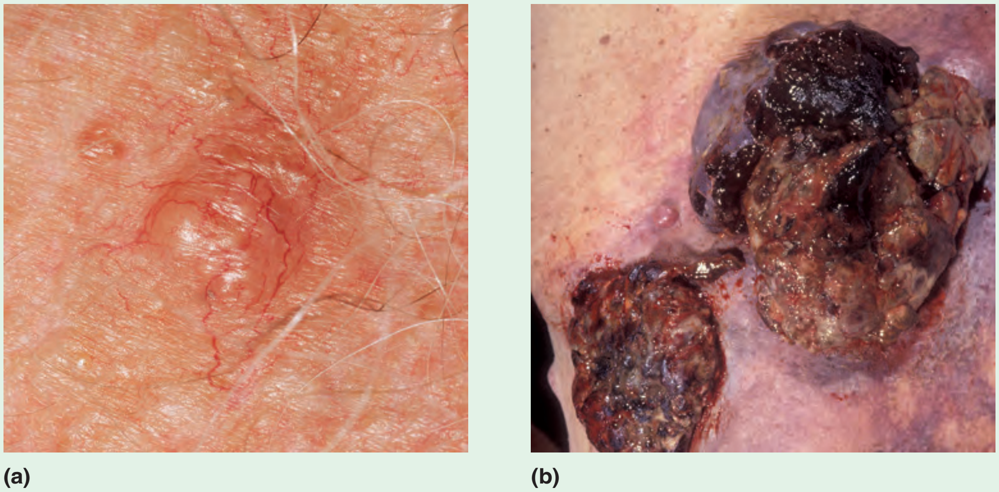

**(a)** **(b)**

**FIGURE 6A** Skin cancer. **(a)** Basal cell carcinoma. **(b)** Malignant melanoma.

Epidermal cells can die if their blood supply from the dermis, which brings nutrients, is blocked. For example, when a person lies in one position for a prolonged period, the weight of the body pressing against the bed blocks the skin's blood supply. If cells die (necrosis), the tissues begin to break down, and a *pressure ulcer* (also called a *decubitus ulcer* or *bedsore*) may appear.

Pressure ulcers usually form in the skin overlying bony projections, such as on the hip, heel, elbow, or shoulder. Frequently changing body position or massaging the skin to stimulate blood flow in regions associated with bony prominences can prevent pressure ulcers.

Nerve cell processes are scattered throughout the dermis. Motor cell processes conduct impulses out from the brain or spinal cord to dermal muscles and glands. Sensory cell processes conduct impulses away from specialized sensory receptors, such as touch receptors in the dermis, and into the brain or spinal cord. Specialized sensory receptors are discussed in chapter 10 (p. 275). The dermis also contains accessory structures including hair follicles, sebaceous (oil-producing) glands, and sweat glands (see fig. 6.1).

To create a tattoo, needles inject inks into the dermis. The color is permanent, because dermal cells are not shed, unlike cells of the epidermis. To remove a tattoo, a laser shatters the ink molecules, and the immune system removes the resulting debris. Before laser removal became available in the late 1980s, unwanted tattoos were scraped, frozen, or cut away—all painful procedures.

**PRACTICE**

10. What types of tissues make up the dermis?
11. What are the functions of these tissues?

## 6.3 | Accessory Structures of the Skin

### Nails

*Nails* are protective coverings on the ends of the fingers and toes. Each nail consists of a *nail plate* that overlies a surface of skin called the *nail bed.* Specialized epithelial cells continuous with the epithelium of the skin produce the nail bed. The whitish, thickened, half-moon–shaped region (lunula) at the base of a nail plate is the most actively growing region. The epithelial cells here divide, and the newly formed cells become keratinized. This gives rise to tiny, keratinized scales that become part of the nail plate, pushing it forward over the nail bed. The keratin of nails is harder than that produced by the epidermal stratum corneum. In time, the nail plate extends beyond the end of the nail bed and with normal use gradually wears away (fig. 6.4).

### Hair Follicles

Hair is present on all skin surfaces except the palms, soles, lips, nipples, and parts of the external reproductive organs. Each hair develops from a group of epidermal stem cells at the base of a tubelike depression called a **hair follicle** (hār fol′i-kl) (figs. 6.1 and 6.5). These stem cells originate from a region near the bottom of the hair follicle known as the *hair bulge*, and migrate downward. The follicle, containing the *hair root*, sometimes extends from the surface through the dermis into the subcutaneous layer. The epidermal cells in the *hair bulb* are nourished from dermal blood vessels in a projection of connective tissue at the deep end of the follicle. As these epidermal cells divide and grow, they push older cells toward the surface. The cells that move upward and away from their nutrient supply become keratinized and die. Their remains constitute the structure of a developing *hair shaft* that extends away from the skin surface (fig. 6.6). In other words, a hair is composed of dead epidermal cells.

Genes determine hair color by directing the type and amount of pigment that epidermal melanocytes produce. Dark hair has more of the brownish-black **eumelanin** (u-mel′ah-nin), while blonde hair and red hair have more of the reddish-yellow **pheomelanin** (fe″o-mel′ah-nin). The white hair of a person with the inherited condition *albinism* lacks melanin altogether. A mixture of pigmented and unpigmented hairs appears gray.

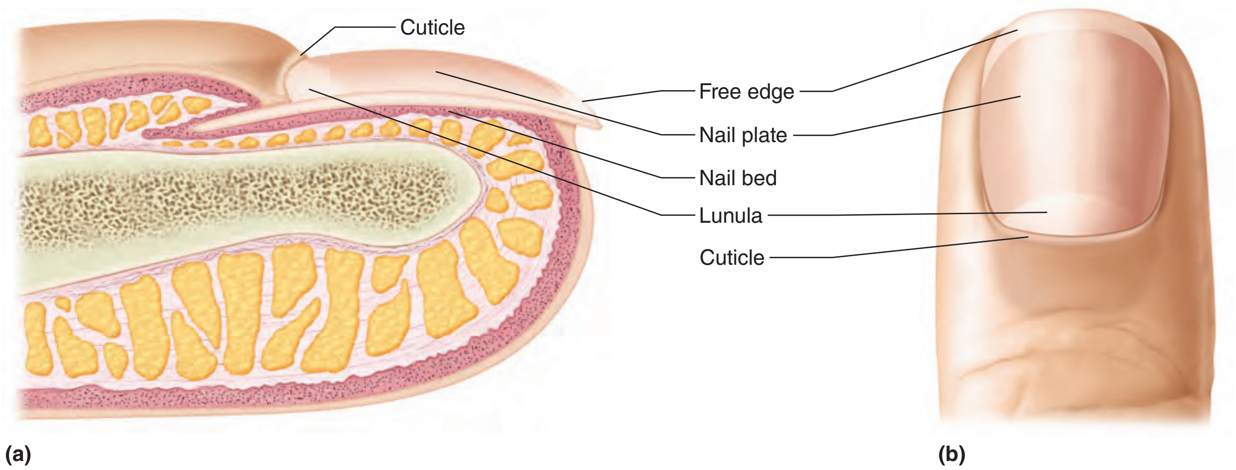


**FIGURE 6.4** Nail. **(a)** Longitudinal section and **(b)** dorsal view of exterior nail.

*What is the most actively growing region of the nail?*

**Answer be found in Appendix F on page 582.**

A bundle of smooth muscle cells, forming the *arrector pili muscle,* attaches to each hair follicle (see figs. 6.1*a* and 6.5*a*). This muscle is positioned so that a short hair within the follicle stands on end when the muscle contracts. If a person is emotionally upset or very cold, nervous stimulation may cause the arrector pili muscles to contract, producing gooseflesh, or goose bumps.

Stem cells from the hair bulge can give rise to epidermal cells of hair or skin. The first clue to the existence of these cells was that new skin in burn patients arises from hair follicles. Manipulating these stem cells could someday treat baldness (alopecia) or extreme hairiness (hirsutism).

## Skin Glands

**Sebaceous glands** (se-ba′shus glandz) contain groups of specialized epithelial cells and are usually associated with hair follicles (figs. 6.5*a* and 6.7). They are holocrine glands (see chapter 5, p. 111) that secrete an oily mixture of fatty material and cellular debris called *sebum* through small ducts into the hair follicles. Sebum helps keep the hair and skin soft, pliable, and waterproof.

Many teens are all too familiar with a disorder of the sebaceous glands called *acne* (acne vulgaris). Overactive and inflamed glands in some body regions become plugged, producing blackheads (comedones), or surrounded by small, red elevations producing pimples (pustules).

**Sweat** (swet) **glands,** or sudoriferous glands, are exocrine glands that are widespread in the skin. Each gland consists of a tiny tube that originates as a ball-shaped coil in the deeper dermis or superficial subcutaneous layer. The coiled portion of the gland is closed at its deep end and is lined with sweat-secreting epithelial cells.

The most numerous **sweat glands,** the **merocrine (eccrine) sweat glands,** respond throughout life to body temperature elevated by environmental heat or

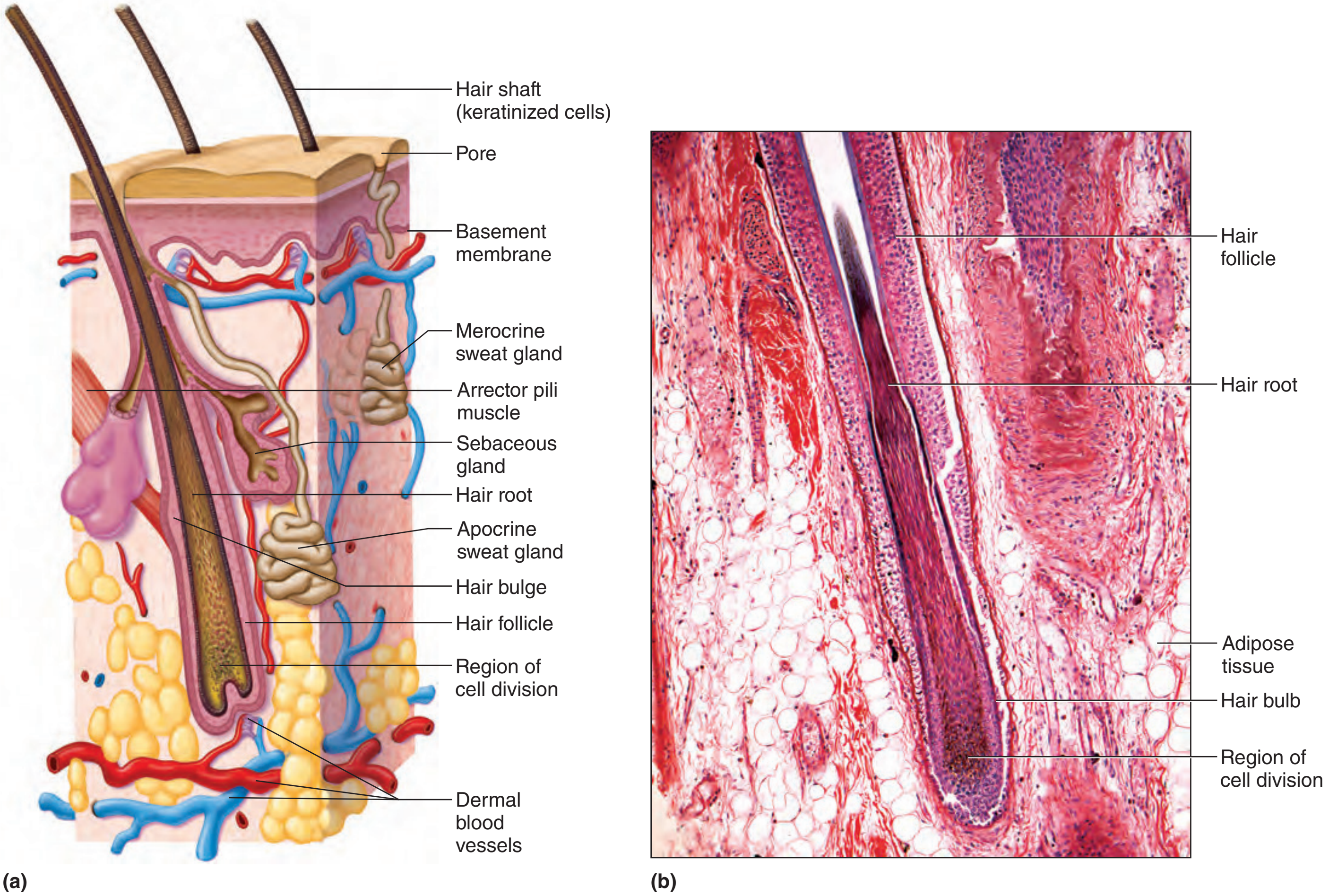

Hair shaft (keratinized cells)
Pore
Basement membrane
Merocrine sweat gland
Arrector pili muscle
Sebaceous gland
Hair root
Apocrine sweat gland
Hair bulge
Hair follicle
Region of cell division
Dermal blood vessels
(a)
Hair follicle
Hair root
Adipose tissue
Hair bulb
Region of cell division
(b)

**FIGURE 6.5** Hair follicle. **(a)** A hair grows from the base of a hair follicle when epidermal cells divide and older cells move outward and become keratinized. **(b)** Light micrograph of a hair follicle (175×).

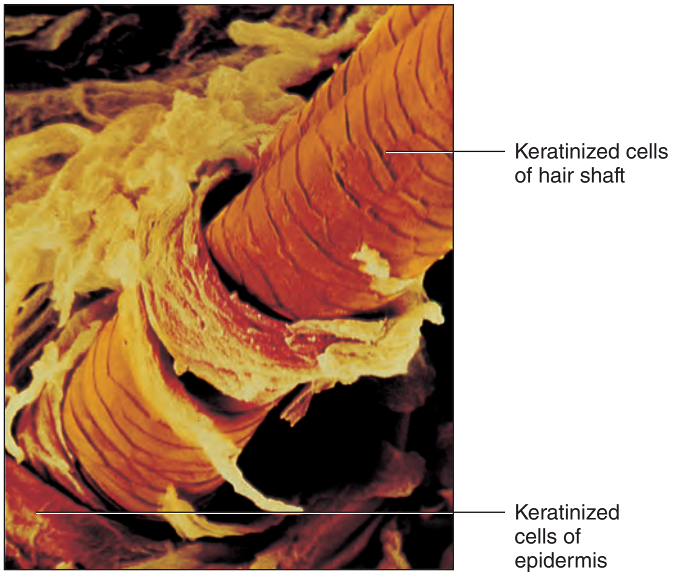

Keratinized cells of hair shaft
Keratinized cells of epidermis

**FIGURE 6.6** APR This scanning electron micrograph shows a hair emerging from the epidermis (875×).

physical exercise (see fig. 6.5*a*). Though located all over the body, these glands are common on the forehead, neck, and back, where they produce profuse sweat on hot days or during intense physical activity. They also release moisture that appears on the palms and soles when a person is emotionally stressed.

The fluid (sweat) that merocrine glands secrete is carried away by a tube (duct) that opens at the surface as a *pore*. Sweat is mostly water, but it also contains small amounts of salt and wastes, such as urea and uric acid. Thus, sweating is also an excretory function.

Other sweat glands, known as **apocrine sweat glands,** become active at puberty. Although they are called apocrine, these glands secrete by exocytosis, usually when a person is emotionally upset, frightened, in pain, or during sexual arousal. The apocrine sweat glands are most numerous in the axillary regions and groin. Ducts of these sweat glands open into hair follicles. The secretions of these sweat glands include proteins and lipids that when metabolized by skin bacteria produce body odor.

Other sweat glands are structurally and functionally modified to secrete specific fluids, such as the *ceruminous glands* of the external ear canal that secrete earwax. The female *mammary glands* that secrete milk are another example of modified sweat glands (see chapter 20, pp. 565–566).

**FACTS OF LIFE** The average square inch (6.45 square centimeters) of skin holds 650 sweat glands, 20 blood vessels, 60,000 melanocytes, and more than a thousand nerve endings.

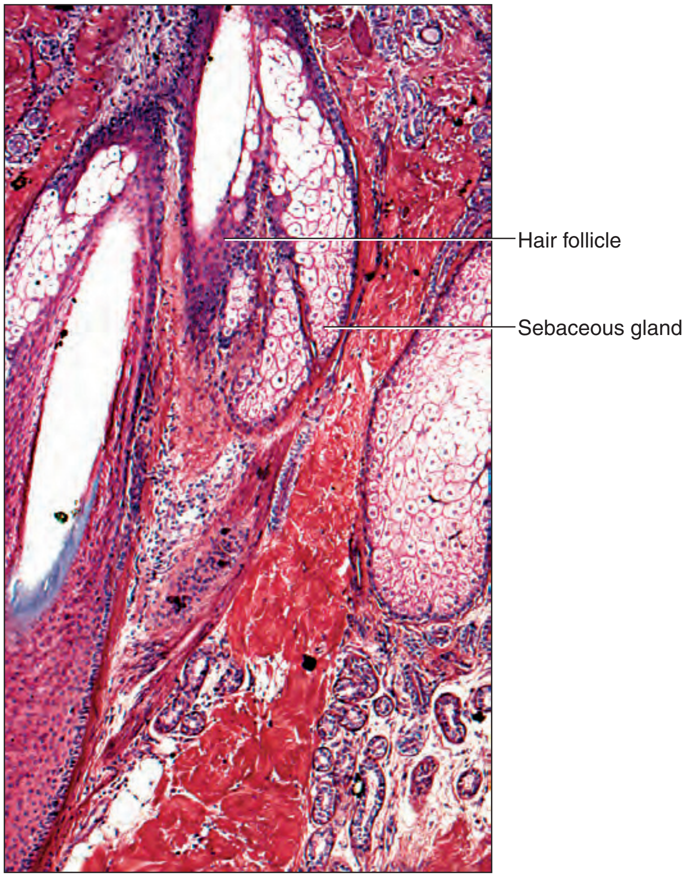


**FIGURE 6.7** APR A sebaceous gland secretes sebum into a hair follicle, shown here in oblique section (200×).

**PRACTICE**

12. Describe the structure of the nail bed.
13. Explain how a hair forms.
14. What is the function of the sebaceous glands?
15. Distinguish between the merocrine and apocrine sweat glands.

## 6.4 Regulation of Body Temperature

Regulation of body temperature is vitally important because even slight shifts can disrupt the rates of metabolic reactions. Normally the temperature of deeper body parts remains close to a set point of 37°C (98.6°F). Maintenance of a stable temperature requires that the amount of heat the body loses be balanced by the amount it produces. The skin plays a key role in the homeostatic mechanism that regulates body temperature.

Heat is a product of cellular metabolism; thus, the more active cells of the body are the major heat producers.

Examples include skeletal and cardiac muscle cells, and cells of the liver.

When body temperature rises above the set point, the nervous system stimulates structures in the skin and other organs to release heat. For example, during physical exercise, active muscles release heat, which the blood carries away. The warmed blood reaches the part of the brain (the hypothalamus) that controls the body's temperature set point, which signals muscles in the walls of dermal blood vessels to relax. As these vessels dilate (vasodilation), more blood enters them, and some of the heat in the blood escapes to the outside.

At the same time as the skin loses heat, the nervous system stimulates the merocrine sweat glands to become active and to release sweat onto the skin surface. As this fluid evaporates (changes from a liquid to a gas), it carries heat away from the surface, cooling the skin.

When body temperature drops below the set point, as may occur in a very cold environment, the brain triggers different responses in the skin structures. Muscles in the walls of dermal blood vessels are stimulated to contract; this decreases the flow of heat-carrying blood through the skin and helps reduce heat loss. Also, the merocrine sweat glands remain inactive, decreasing heat loss by evaporation. If body temperature continues to drop, the nervous system may stimulate muscle cells in the skeletal muscles throughout the body to contract slightly. This action requires an increase in the rate of cellular respiration, which releases heat as a by-product. If this response does not raise body temperature to normal, small groups of muscles may rhythmically contract with greater force, causing the person to shiver, generating more heat. Chapter 1 introduced this homeostatic mechanism (fig. 1.7, p. 16).

Deviation from the normal range for body temperature may have dangerous consequences. People with severe spinal cord injuries can no longer control body temperature, which fluctuates depending upon the environment. The very young with undeveloped nervous systems have difficulty regulating their body temperature. The very old may have less adipose tissue in the subcutaneous layer beneath the skin (less insulation).

In hypothermia, core body temperature falls below 95°F. Hypothermia initially produces shivering and a feeling of coldness. Symptoms of worsening hypothermia include a gradual loss of coordination, stiffening muscles, confusion, fatigue, and slow, shallow breathing. When core temperature falls to 87.8°F, the skin turns a bluish-gray, weakness intensifies, and consciousness fades.

In hyperthermia, core body temperature exceeds 101°F. The skin becomes hot, dry, and flushed, and the person becomes weak, dizzy, and nauseous, with headache and a rapid, irregular pulse. The vignette that opens chapter 18 (p. 502) describes heatstroke.

## PRACTICE

16. Why is regulation of body temperature so important?
17. How does the body lose excess heat?
18. Which actions help the body conserve heat?

## 6.5 | Healing of Wounds

A wound and the area surrounding it usually become red and painfully swollen. This is the result of *inflammation,* which is a normal response to injury or stress. Blood vessels in affected tissues dilate and become more permeable, allowing fluids to leak into the damaged tissues. Inflamed skin may become reddened, warm, swollen, and painful to touch (table 6.1). However, the dilated blood vessels provide the tissues with more nutrients and oxygen, which aids healing.

The specific events in the healing process depend on the nature and extent of the injury. If a break in the skin is shallow, epithelial cells along its margin are stimulated to divide more rapidly than usual, and the newly formed cells fill the gap.

If the injury extends into the dermis or subcutaneous layer, blood vessels break, and the released blood forms a clot in the wound. The blood clot and the dried tissue fluids form a *scab* that covers and protects underlying tissues. Before long, fibroblasts migrate into the injured region and begin secreting collagen fibers that bind the edges of the wound. Suturing (stitching) or otherwise closing a large break in the skin speeds this process.

As healing continues, blood vessels extend into the area beneath the scab. Phagocytic cells remove dead cells and other debris. Eventually, the damaged tissues are replaced, and the scab sloughs off. In some cases, extensive production of collagen fibers may form an elevation above the normal epidermal surface, called a *scar.*

In large, open wounds, healing may be accompanied by formation of small, rounded masses called *granulations* that develop in the exposed tissues. A granulation consists of a new branch of a blood vessel

**TABLE 6.1 Inflammation**

| Symptom | Cause |
|---|---|
| Redness | Vasodilation, more blood in area |
| Heat | Large amount of blood accumulating in area and as a by-product of increased metabolic activity in tissue |
| Swelling | Increased permeability of blood vessels, fluids leaving blood go into tissue spaces (edema) |
| Pain | Injury to neurons and increased pressure from edema |

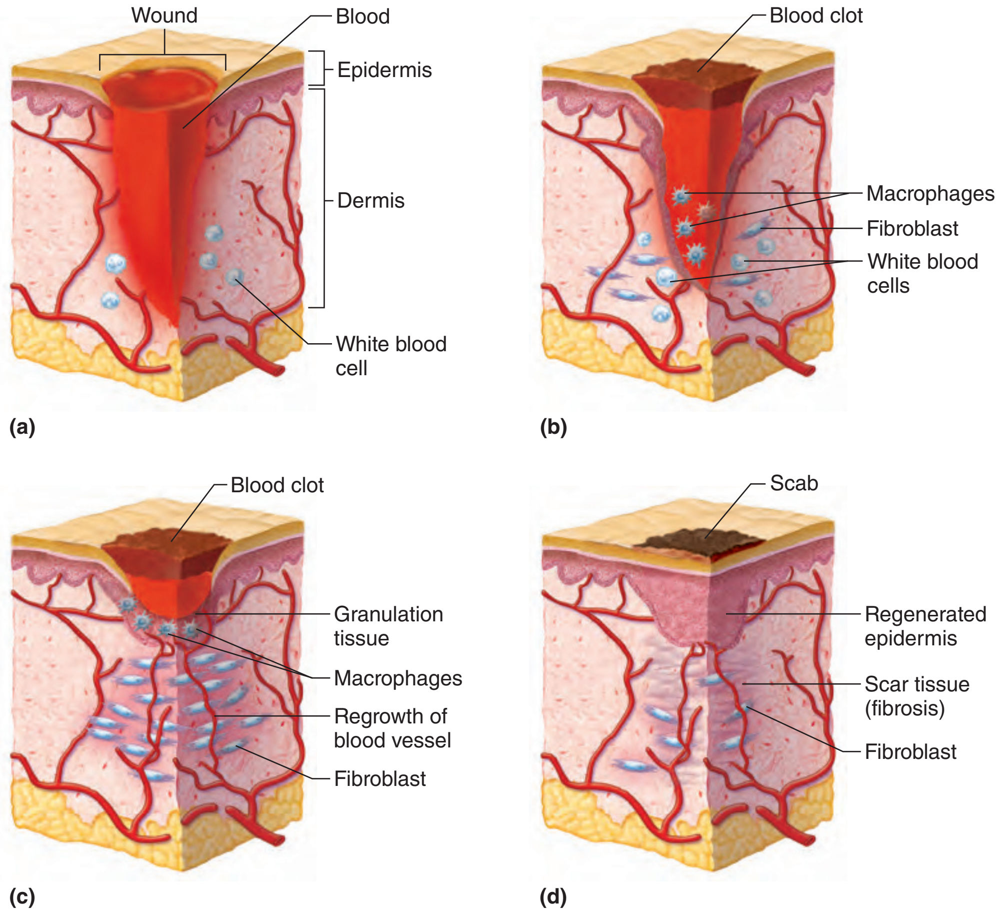


**FIGURE 6.8 Healing of a wound.** **(a)** When skin is injured, blood escapes from dermal blood vessels, and **(b)** a blood clot soon forms. **(c)** Blood vessels send out branches, and fibroblasts migrate into the area. The fibroblasts produce collagen fibers. **(d)** The scab formed by the blood clot and dried tissue fluid protects the damaged region until the skin is mostly repaired. Then, the scab sloughs off. Scar tissue continues to form, elevating the epidermal surface. (Note: The cells are not drawn to scale.)

and a cluster of collagen-secreting fibroblasts that the vessel nourishes. In time, some of the blood vessels are resorbed, and the fibroblasts move away, leaving a scar largely composed of collagen fibers. Figure 6.8 shows the stages in the healing of a wound. Clinical Application 6.2 describes healing of burned tissue.

## PRACTICE

19. What is the tissue response to inflammation?
20. Distinguish between the activities necessary to heal a wound in the epidermis and those necessary to heal a wound in the dermis.
21. Explain the role of phagocytic cells in wound healing.
22. Define *granulation.*

## COMMON SKIN DISORDERS

**acne** (ak′ne) Disease of the sebaceous glands that produces blackheads and pimples.

**alopecia** (al″o-pe′she-ah) Hair loss, usually sudden.

**athlete's foot** (ath′-lētz foot) Fungus (*Tinea pedis*) infection usually in the skin of the toes and soles.

**birthmark** (berth′ mark) Congenital blemish or spot on the skin, visible at birth or soon after.

**boil** (boil) Bacterial infection (furuncle) of the skin, produced when bacteria enter a hair follicle.

**carbuncle** (kar′bung-kl) Bacterial infection, similar to a boil, that spreads into the subcutaneous tissues.

**cyst** (sist) Liquid-filled sac or capsule.

**dermatitis** (der″mah-ti′tis) Inflammation of the skin.

**eczema** (ek′zĕ-mah) Noncontagious skin rash that produces itching, blistering, and scaling.

**erythema** (er″ĭ-the′mah) Reddening of the skin due to dilation of dermal blood vessels in response to injury or inflammation.

**herpes** (her′pēz) Infectious disease of the skin, caused by the herpes simplex virus and characterized by recurring formations of small clusters of vesicles.

**impetigo** (im″pĕ-ti′go) Contagious disease of bacterial origin, characterized by pustules that rupture and become covered with loosely held crusts.

**keloid** (ke′loid) Elevated, enlarging fibrous scar usually initiated by an injury.

**mole** (mōl) Benign skin tumor (nevus) that is usually pigmented; colors range from brown to black.

**pediculosis** (pĕ-dik″u-lo′sis) Disease produced by an infestation of lice.

## CLINICAL APPLICATION 6.2

## Burns

A few hours outside on a sunny summer day, without use of sunscreen, may result in a minor sunburn. The slightly burned skin becomes inflamed, it warms and reddens (erythema) as dermal blood vessels dilate. Mild edema may swell the exposed tender skin, and a few days later the surface layer of skin may peel. Any burn injuring only the epidermis is a *superficial partial-thickness* (first degree) *burn*. Healing usually takes a few days to two weeks, with no scarring.

A burn that destroys some epidermis as well as some underlying dermis is a *deep partial-thickness* (second degree) *burn*. Fluid escapes from damaged dermal capillaries, accumulating beneath the outer layer of epidermal cells, forming blisters. The injured region becomes moist and firm and may vary from dark red to waxy white. Such a burn most commonly occurs as a result of exposure to hot objects, hot liquids, flames, or burning clothing.

The extent of healing of a deep partial-thickness burn depends upon stem cells that are associated with accessory structures of the skin. These structures include hair follicles, sweat glands, and sebaceous glands. They survive the injury because although they are derived from the epidermis, they extend into the dermis. During healing, the stem cells divide, and their daughter cells grow out onto the surface of the exposed dermis, spread over it and differentiate as new epidermis.

A burn that destroys the epidermis, the dermis, and the accessory structures of the skin is a *full-thickness* (third degree) *burn*. The injured skin becomes dry and leathery, and it may vary in color from red to black to white. A full-thickness burn usually results from immersion in hot liquids, prolonged exposure to hot objects, flames, or corrosive chemicals. Because most of the epithelial cells in the affected region are destroyed, healing occurs by growth of epithelial cells inward from the margin of the burn. If the injured area is extensive, it may require a transplant, using a thin layer of skin from an unburned region of the body (an autograft), cadaveric skin (a homograft), or a skin substitute such as tissue-engineered skin (fig. 6B).

The treatment of a burn patient requires estimating the extent of the body's affected surface. Physicians use the "rule of nines," subdividing the skin's surface into regions, each accounting for 9% (or some multiple of 9%) of the total surface area (fig. 6C). This estimate is important in planning to replace body fluids and electrolytes lost from injured tissues and for covering the burned area with skin or skin substitutes.

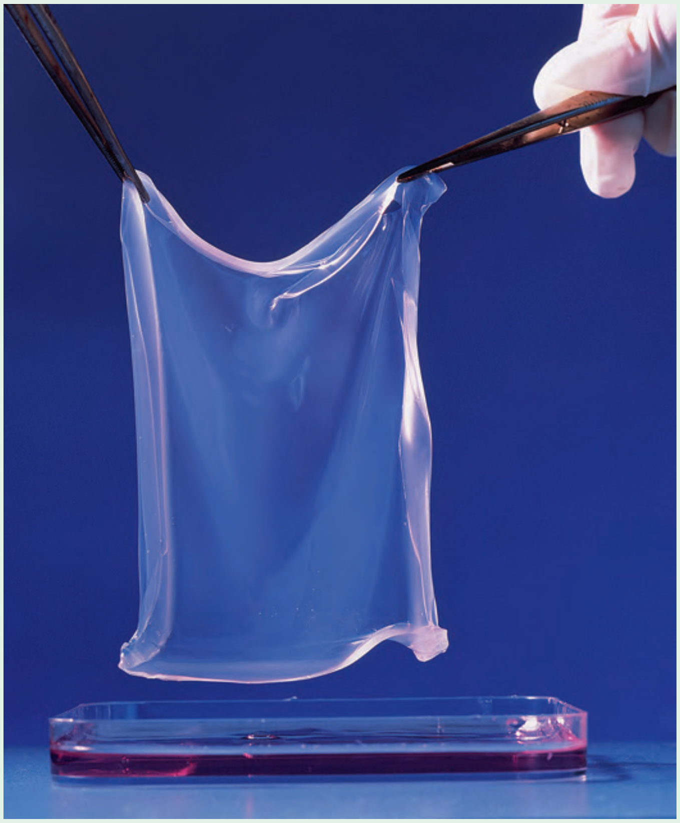


**FIGURE 6B** Artificial skin typically consists of a collagen framework seeded with a patient's own skin cells.

**pruritus** (proo-ri′tus) Itching of the skin.
**psoriasis** (so-ri′ah-sis) Chronic skin disease characterized by red patches covered with silvery scales.
**pustule** (pus′tūl) Elevated, pus-filled area on the skin.
**scabies** (ska′bēz) Disease resulting from an infestation of mites.
**seborrhea** (seb″o-re′ah) Hyperactivity of the sebaceous glands, causing greasy skin and dandruff.
**ulcer** (ul′ser) Open sore.
**urticaria** (ur″tĭ-ka′re-ah) Allergic reaction of the skin that produces reddish, elevated patches (hives).
**vitiligo** (vit′ĭ-li′go) Loss of melanocytes in parts of the epidermis, producing whitened areas of skin.
**wart** (wort) Flesh-colored, raised area caused by a viral infection.

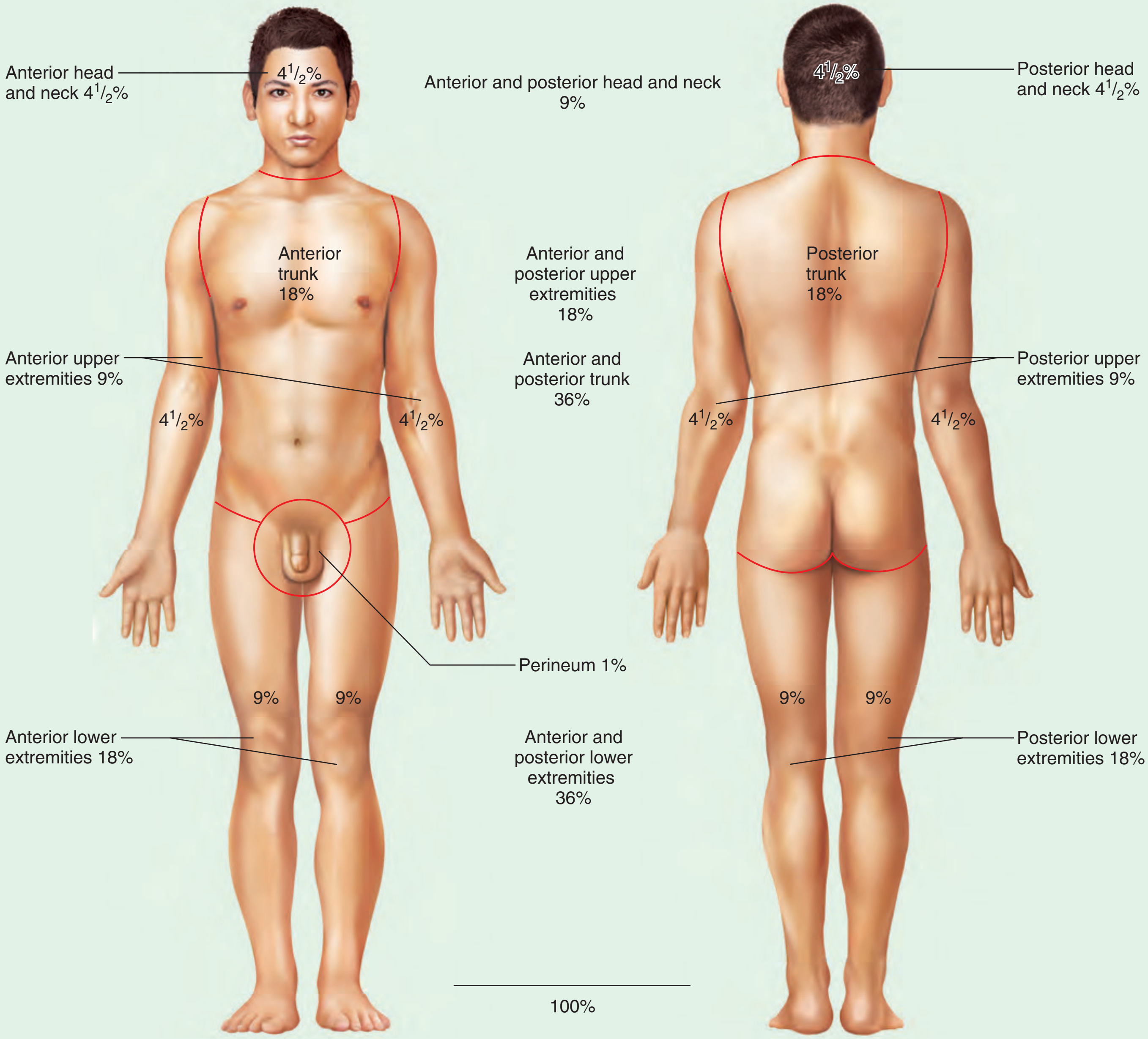

Anterior head and neck 4½%
4½%
Anterior and posterior head and neck 9%
4½%
Posterior head and neck 4½%
Anterior trunk 18%
Anterior and posterior upper extremities 18%
Posterior trunk 18%
Anterior upper extremities 9%
Anterior and posterior trunk 36%
Posterior upper extremities 9%
4½%
4½%
4½%
4½%
Perineum 1%
9%
9%
9%
9%
Anterior lower extremities 18%
Anterior and posterior lower extremities 36%
Posterior lower extremities 18%
100%

**FIGURE 6C** As an aid for estimating the extent of damage burns cause, the body is subdivided into regions, each representing 9% (or some multiple of 9%) of the total skin surface area.

# Integumentary System

The skin provides protection, contains sensory receptors, and helps control body temperature.

## Skeletal System

Vitamin D, production of which begins in the skin, helps provide calcium needed for bone matrix.

## Muscular System

Involuntary muscle contractions (shivering) work with the skin to control body temperature. Muscles act on facial skin to create expressions.

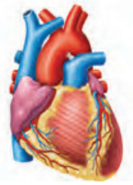
## Nervous System

Sensory receptors provide information about the outside world to the nervous system. Nerves control the activity of sweat glands.

## Endocrine System

Hormones help to increase skin blood flow during exercise. Other hormones stimulate either the synthesis or the decomposition of subcutaneous fat.

## Cardiovascular System



Skin blood vessels play a role in regulating body temperature.

## Lymphatic System

The skin, acting as a barrier, provides an important first line of defense for the immune system.

## Digestive System

Excess calories may be stored as subcutaneous fat. Vitamin D, production of which begins in the skin, stimulates dietary calcium absorption.

## Respiratory System

Stimulation of skin receptors may alter respiratory rate.

## Urinary System

The kidneys help compensate for water and electrolytes lost in sweat.

## Reproductive System

Sensory receptors play an important role in sexual activity and in the suckling reflex.

## Summary Outline

### 6.1 Introduction (p. 128)

*An organ is formed by two or more tissue types grouped together and performing specialized functions. The skin, the largest organ in the body by weight, is part of the integumentary system.*

### 6.2 Skin and Its Tissues (p. 128)

*Skin is a protective covering, helps regulate body temperature, retards water loss, houses sensory receptors, synthesizes various biochemicals, and excretes wastes. It is composed of an epidermis and a dermis separated by a basement membrane. Beneath the skin is the subcutaneous layer that binds the skin to underlying organs, stores fat, and contains blood vessels that supply the skin.*

1. Epidermis
    - a. The epidermis is stratified squamous epithelium that lacks blood vessels.
    - b. The deepest layer of the epidermis, called the stratum basale, contains cells that divide.
    - c. Epidermal cells undergo keratinization as they mature and are pushed toward the surface.
    - d. The outermost layer, called the stratum corneum, is composed of dead epidermal cells.
    - e. The epidermis protects underlying tissues against water loss, mechanical injury, and the effects of harmful chemicals.
    - f. Melanin protects underlying cells from the effects of ultraviolet light.
    - g. Melanocytes transfer melanin to nearby epidermal cells.
    - h. Melanin provides skin color.
        - (1) All people have about the same number of melanocytes.
        - (2) Skin color is due largely to the amount of melanin and the distribution and size of pigment granules in the epidermis.
        - (3) Environmental and physiological factors, as well as genes, influence skin color.
2. Dermis
    - a. The dermis binds the epidermis to underlying tissues.
    - b. Dermal blood vessels supply nutrients to all skin cells and help regulate body temperature.
    - c. Nerve cell processes are scattered throughout the dermis.
        - (1) Some dermal nerve cell processes conduct impulses to muscles and glands of the skin.
        - (2) Other dermal nerve cell processes are associated with sensory receptors in the skin, and conduct impulses to the brain and spinal cord.
    - d. The dermis also has hair follicles, sebaceous glands, and sweat glands.

### 6.3 Accessory Structures of the Skin (p. 133)

1. Nails
    - a. Nails are protective covers on the ends of fingers and toes.
    - b. Specialized epidermal cells that are keratinized make up nails.
    - c. The keratin of nails is harder than that produced by the skin's epidermal cells.
2. Hair follicles
    - a. Each hair develops from epidermal cells at the base of a tubelike hair follicle.
    - b. As newly formed cells develop and grow, older cells are pushed toward the surface and undergo keratinization.
    - c. Hair color is determined by genes that direct the amount of eumelanin or pheomelanin produced by melanocytes associated with hair follicles.
    - d. A bundle of smooth muscle cells is attached to each hair follicle.
3. Skin glands
    - a. Sebaceous glands are usually associated with hair follicles.
    - b. Sebaceous glands secrete sebum, which helps keep the skin and hair soft and waterproof.
    - c. Each sweat gland is a coiled tube.
    - d. Merocrine sweat glands respond to elevated body temperature, and produce sweat that is primarily water but also contains salts and wastes.
    - e. Apocrine sweat glands respond to emotional upset and produce sweat containing proteins and lipids.

### 6.4 Regulation of Body Temperature (p. 135)

*Regulation of body temperature is vital because heat affects the rates of metabolic reactions. Normal temperature of deeper body parts is close to a set point of 37°C (98.6°F).*

1. When body temperature rises above the normal set point, dermal blood vessels dilate and sweat glands secrete sweat.
2. When body temperature drops below the normal set point, dermal blood vessels constrict and sweat glands become inactive.
3. If body temperature continues to drop, skeletal muscles involuntarily contract.

### 6.5 Healing of Wounds (p. 136)

*Skin injuries trigger inflammation. The affected area becomes red, warm, swollen, and tender.*

1. Dividing epithelial cells fill in shallow cuts in the epidermis.
2. Clots close deeper cuts, sometimes leaving a scar where connective tissue replaces skin.
3. Granulations form in large, open wounds as part of the healing process.

## CHAPTER ASSESSMENTS

### 6.1 Introduction

**1.** Two or more types of tissues grouped together and performing specialized functions defines a(n) ____________. (p. 128)

a. organelle
b. cell
c. organ
d. organ system

**2.** The largest organ(s) in the body, by weight, is (are) the __________. (p. 128)

a. liver
b. intestines
c. lungs
d. skin

### 6.2 Skin and Its Tissues

**3.** Functions of the skin include ____________. (p. 128)

a. excretion
b. body temperature regulation
c. sensory reception
d. all of the above

**4.** Describe how skin plays a role in the production of vitamin D. (p. 128)

**5.** The epidermis on the soles of the feet is composed of layers of ________ tissue. (p. 130)

6. The ____________ layer of epidermal cells contains older keratinized cells and dead cells. (p. 130)
   a. stratum corneum
   b. stratum granulosum
   c. stratum spinosum
   d. stratum basale
7. Discuss the function of melanin, other than providing color to the skin. (p. 130)
8. List and describe the influence of each factor affecting skin color. (p. 130)
9. Name the tissue(s) that make up the dermis. (p. 131)

**6.3 Accessory Structures of the Skin**

10. Describe how nails are formed, and relate the structure of nails to their function. (p. 133)
11. Distinguish between a hair and a hair follicle. (p. 133)
12. Sebaceous glands are _________ glands that secrete _________. (p. 134)
13. Compare and contrast merocrine and apocrine sweat glands. (pp. 134–135)

**6.4 Regulation of Body Temperature**

14. Explain how body heat is produced. (p. 135)
15. Explain how sweat glands help regulate body temperature. (p. 136)
16. Describe the body's responses to decreasing body temperature. (p. 136)

**6.5 Healing of Wounds**

17. Explain how the healing of superficial breaks in the skin differs from the healing of deeper wounds. (p. 136)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 5.3, 6.2, 6.4

1. A premature infant typically lacks subcutaneous adipose tissue. Also, the surface area of an infant's body is relatively large compared to its volume. How do these factors affect the ability of a premature infant to regulate its body temperature?

### OUTCOME 6.2

2. Which of the following would result in the more rapid absorption of a drug: a subcutaneous injection or an intradermal injection? Why?
3. Everyone's skin contains about the same number of melanocytes, even though people have many different skin colors. How is this possible?

### OUTCOMES 6.2, 6.3, 6.4, 6.5

4. Using the rule of nines, estimate the extent of damage for an individual whose body, clad only in a short nightgown, was burned as she was leaving the burning room. What special problems would result from the loss of 50% of a person's functional skin surface? How might this person's environment be modified to partially compensate for such a loss?

### OUTCOMES 6.2, 6.5

5. How is it protective for skin to peel after a severe sunburn?
6. As a rule, a superficial partial-thickness burn is more painful than one involving deeper tissues. How would you explain this observation?

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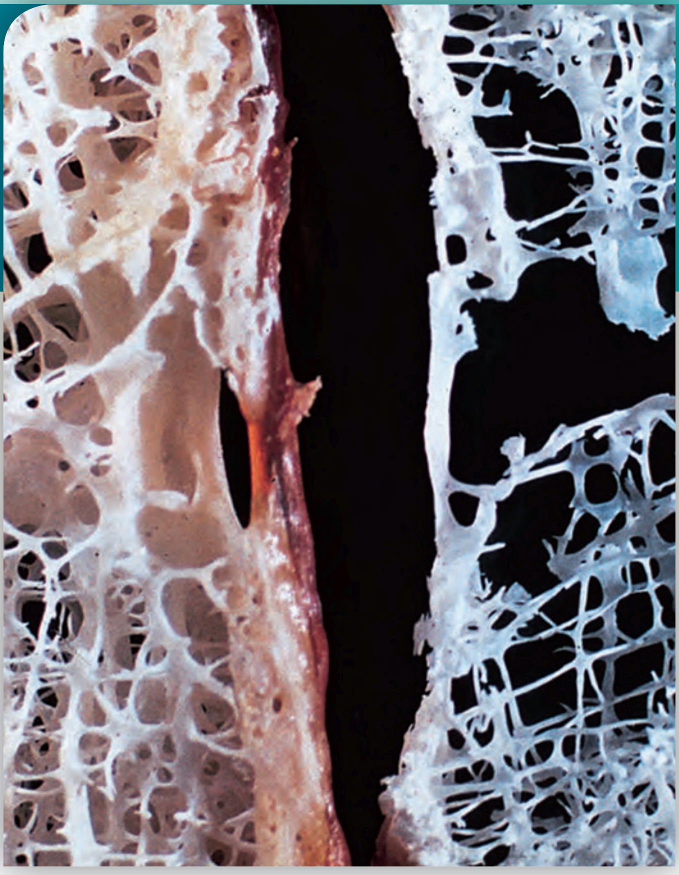
# 7

# Skeletal System



*Spaces in bones enlarge when a person has osteoporosis. The portion of a vertebra on the left is normal; the one on the right has been weakened by osteoporosis.*

Preventing "fragility fractures." Skeletal health is a matter of balance. Before age thirty, cells that form new bone counter cells that break it down, so that living bone is in a constant state of remodeling. Then the balance shifts so that bone is lost, especially in women past menopause, due to hormonal changes. This imbalance may progress to osteopenia or the more severe osteoporosis.

A condition called "fragility fracture" is a sign of dangerously low bone density. This is a fracture that happens after a fall from less than standing height, which a strong, healthy skeleton could resist. Fragility fractures occur in 1.5 million people in the United States each year, yet despite this warning sign, only one-fourth to one-third of them are followed up with bone scans and treatment to build new bone. Several drugs are used to treat osteoporosis. One class, the bisphosphonates, actually builds new bone.

Osteopenia and osteoporosis are common. The surgeon general estimates that half of all people over age fifty have one of these conditions, which amounts to 10 million with osteoporosis and another 35 million with osteopenia. Screening is advised for all individuals over age sixty-five, as well as for those with risk factors. The strongest predictor is a previous fragility fracture. Other risk factors include a family history of osteoporosis, recent height loss, and older age.

These two conditions are not just concerns of older people. Researchers think that what puts people at risk is failure to attain maximal possible bone density by age thirty. To keep bones as strong as possible for as long as possible, it is essential to exercise for at least 30 minutes daily (some of which should be weight-bearing), consume enough daily calcium (1,000–1,200 mg) and vitamin D (200–600 IU), according to the American Academy of Orthopaedic Surgeons, and not smoke. There is much a person can do to promote skeletal health—at any age.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 7.1 Introduction

1. List the active tissues found in a bone. (p. 144)

### 7.2 Bone Structure

2. Describe the macroscopic and microscopic structure of a long bone, and list the functions of these parts. (pp. 144–146)

### 7.3 Bone Development and Growth

3. Distinguish between intramembranous and endochondral bones, and explain how such bones develop and grow. (pp. 146–148)

### 7.4 Bone Function

4. Discuss the major functions of bones. (pp. 149 and 152)

### 7.5 Skeletal Organization

5. Distinguish between the axial and appendicular skeletons, and name the major parts of each. (pp. 153–154)

### 7.6–7.12 Skull—Lower Limb

6. Locate and identify the bones and the major features of the bones that compose the skull, vertebral column, thoracic cage, pectoral girdle, upper limb, pelvic girdle, and lower limb. (pp. 155–174)

### 7.13 Joints

7. Classify joints according to the type of tissue binding the bones together, describe the different joint characteristics, and name an example of each joint type. (p. 174)
8. List six types of synovial joints, and describe the actions of each. (p. 175)
9. Explain how skeletal muscles produce movements at joints, and identify several types of joint movements. (pp. 178–180)

**Module 5:**
Skeletal System

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**acetabul-** [vinegar cup] *acetabul*um: Depression of the hip bone that articulates with the head of the femur.

**ax-** [axis] *ax*ial skeleton: Bones of the cranium, vertebral column, ribs, and sternum.

**-blast** [bud] osteo*blast*: Cell that will form bone tissue.

**carp-** [wrist] *carp*als: Wrist bones.

**-clast** [break] osteo*clast*: Cell that breaks down bone tissue.

**condyl-** [knob] *condyl*e: Rounded, bony process.

**corac-** [a crow's beak] *corac*oid process: Beaklike process of the scapula.

**cribr-** [sieve] *cribr*iform plate: Portion of the ethmoid bone with many small openings.

**crist-** [crest] *crist*a galli: Bony ridge that projects upward into the cranial cavity.

**fov-** [pit] *fov*ea capitis: Pit in the head of a femur.

**glen-** [joint socket] *glen*oid cavity: Depression in the scapula that articulates with the head of a humerus.

**inter-** [among, between] *inter*vertebral disc: Structure between vertebrae.

**intra-** [inside] *intra*membranous bone: Bone that forms within sheetlike masses of connective tissue.

**meat-** [passage] external acoustic *meat*us: Canal of the temporal bone that leads inward to parts of the ear.

**odont-** [tooth] *odont*oid process: Toothlike process of the second cervical vertebra.

**poie-** [make, produce] hemato*poie*sis: Process that forms blood cells.

---

## 7.1 | Introduction

A bone may appear to be inert because of nonliving material in the extracellular matrix of bone tissue. However, bone tissue, cartilage, dense connective tissue, blood, and nervous tissue are very much alive and active. Bones are not only alive but also multifunctional. Bones and organs of the **skeletal system** support and protect softer tissues, provide points of attachment for muscles, house blood-producing cells, and store inorganic salts.

**PRACTICE**

1. Name the living tissues in bone.

## 7.2 | Bone Structure

The bones of the skeletal system differ greatly in size and shape. However, they are similar in structure, development, and function.

### Bone Classification

Bones are classified according to their shapes—long, short, flat, or irregular.

- **Long bones** have long longitudinal axes and expanded ends. Examples of long bones are the forearm and thigh bones.
- **Short bones** are somewhat cubelike, with roughly equal lengths and widths. The bones of the wrists and ankles are this type. A special type of short bone is a **sesamoid bone** or **round bone**. This type of bone is usually small and nodular and develops within a tendon or adjacent to a joint. The kneecap (patella) is a sesamoid bone.
- **Flat bones** are platelike structures with broad surfaces, such as the ribs, the scapulae, and some bones of the skull.
- **Irregular bones** have a variety of shapes and most are connected to several other bones. Irregular bones include the vertebrae that compose the backbone, and many facial bones.

### Parts of a Long Bone

The femur, the long bone in the thigh, illustrates the structure of bone (fig. 7.1). At each end of a long bone is an expanded portion called an **epiphysis** (e-pif′ĭ-sis) (plural, *epiphyses*), which articulates (forms a joint) with another bone. The epiphysis that is nearest the attachment to the trunk of the body is called the proximal epiphysis. The one that is farthest from the trunk of the body is called the distal epiphysis. On its outer surface, the articulating portion of the epiphysis is coated with a layer of hyaline cartilage called **articular cartilage** (ar-tik′u-lar kar′tĭ-lij). The shaft of the bone, between the epiphyses, is called the **diaphysis** (di-af′ĭ-sis).

A tough covering of dense connective tissue called the **periosteum** (per″e-os′te-um) completely encloses the bone, except for the articular cartilage on the bone's ends. The periosteum is firmly attached to the bone, and periosteal fibers are continuous with the connecting ligaments and tendons. The periosteum also helps form and repair bone tissue.

A bone's shape makes possible the bone's functions. For example, bony projections called *processes* provide sites where ligaments and tendons attach; grooves and openings form passageways for blood vessels and nerves; and a depression of one bone may articulate with a process of another.

The wall of the diaphysis is mainly composed of tightly packed tissue called **compact bone** (kom′pakt bōn), or cortical bone. This type of bone has a continu-

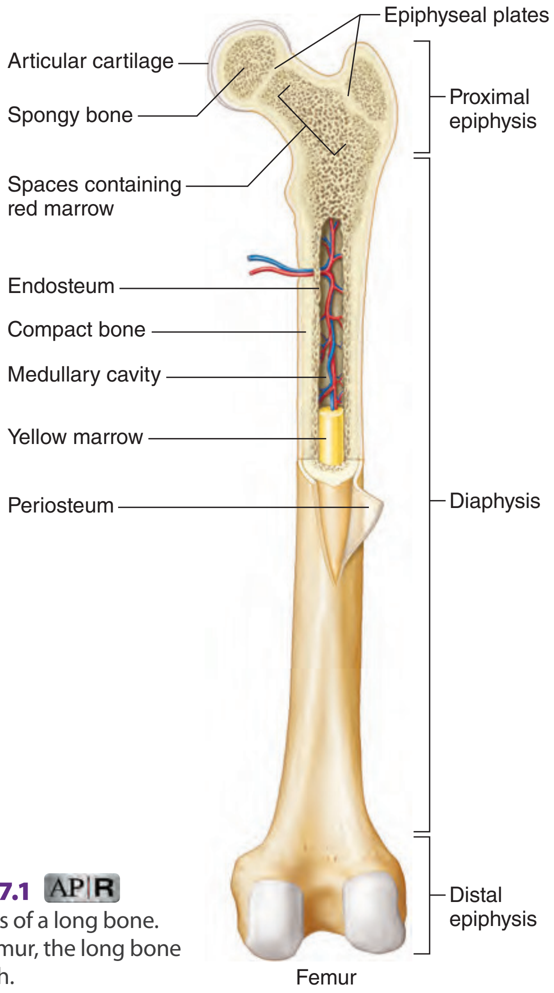


**FIGURE 7.1** AP|R Major parts of a long bone. This is a femur, the long bone in the thigh.

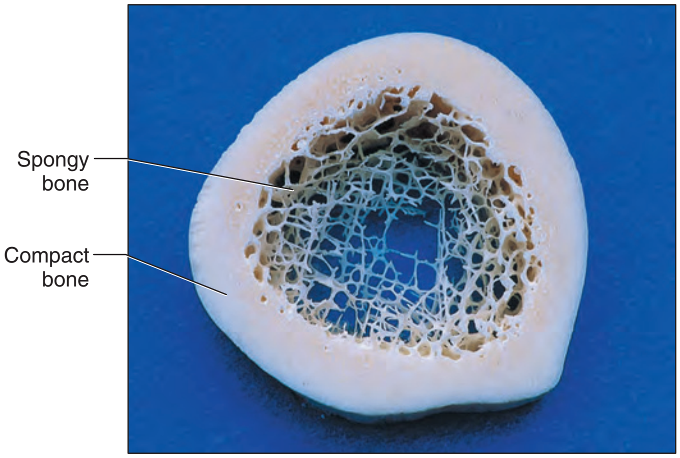


**FIGURE 7.2** AP|R This cross section of a long bone reveals a layer of spongy bone beneath a layer of compact bone.

ous extracellular matrix with no gaps. The epiphyses, in contrast, are composed largely of **spongy bone** (spun′je bōn), or cancellous bone, with thin layers of compact bone on their surfaces. Spongy bone consists of numerous branching bony plates called **trabeculae** (trah-bek′u-le). Irregular connecting spaces between these plates help reduce the bone's weight (fig. 7.2). The bony plates are most highly developed in the regions of the epiphyses that are subjected to compressive forces. Both compact and spongy bone are strong and resist bending.

Compact bone in the diaphysis of a long bone forms a tube with a hollow chamber called the **medullary cavity** (med′u-lār″e kav′ĭ-te) that is continuous with the spaces of the spongy bone. A thin layer of cells called the **endosteum** (en-dos′te-um) lines these areas, and a specialized type of soft connective tissue called **marrow** (mar′o) fills them.

## Microscopic Structure

Recall from chapter 5 (p. 119) that bone cells called *osteocytes* occupy very small, bony chambers called *lacunae,* which form concentric circles around *central canals* (Haversian canals). Osteocytes exchange substances with nearby cells by means of cellular processes passing through *canaliculi* (fig. 7.3; see fig. 5.20, p. 120). The extracellular matrix of bone tissue is largely collagen and inorganic salts (calcium phosphate). Collagen gives bone its strength and resilience, and inorganic salts make it hard and resistant to crushing.

### CAREER CORNER

### Radiologic Technologist

At age fifty-two the woman is younger than most of the others having their bone mineral density measured. The gynecologist advised a baseline test to assess the health of the patient's skeleton because her parents had osteoporosis.

A radiology technologist conducts the test. She explains the test to the patient, then positions her on her back on a padded table, fully clothed. The scanner passes painlessly over the patient's hip and lower spine, emitting low-dose X rays that form images of the bones. Spaces indicate osteopenia, the low bone mineral density that may be a prelude to osteoporosis.

Radiology technologists administer medical imaging tests, such as ultrasound and magnetic resonance imaging (MRI), as well as mammography and the three-dimensional X-ray cross sections of computerized tomography (CT). They protect patients from radiation with drapes and positioning and operate scanning devices to produce the highest-quality images, from which a radiologist can accurately diagnose an illness or injury.

A registered radiologic technologist completes two years of training at a hospital or a two- or four-year program at a college or university, and must pass a national certification exam.

In compact bone, the osteocytes and layers of extracellular matrix concentrically clustered around a central canal form a cylinder-shaped unit called an *osteon* (Haversian system). Many of these units together form the substance of compact bone.

Each central canal contains blood vessels and nerve fibers surrounded by loose connective tissue. Blood in these vessels nourishes bone cells associated with the central canal.

Central canals extend longitudinally through bone tissue, and transverse *perforating canals* (Volkmann's canals) connect them. Perforating canals contain larger blood vessels and nerves by which the smaller blood vessels and nerve fibers in central canals communicate with the surface of the bone and the medullary cavity (fig. 7.3).

Spongy bone is also composed of osteocytes and extracellular matrix, but the bone cells do not aggregate around central canals. Instead, the cells lie in the *trabeculae* and get nutrients from substances diffusing into canaliculi that lead to the surface of these thin, bony plates.

**PRACTICE**

2. Explain how bones are classified.
3. List five major parts of a long bone.
4. How do compact and spongy bone differ in structure?
5. Describe the microscopic structure of compact bone.

## 7.3 | Bone Development and Growth

Parts of the skeletal system begin to form during the first few weeks of prenatal development, and bony structures continue to develop and grow into adulthood. Bones form by replacing existing connective tissues in either of two ways: (1) Intramembranous bones originate between sheetlike layers of connective tissues; (2) Endochondral bones begin as masses of hyaline cartilage that are later replaced by bone tissue (fig. 7.4).

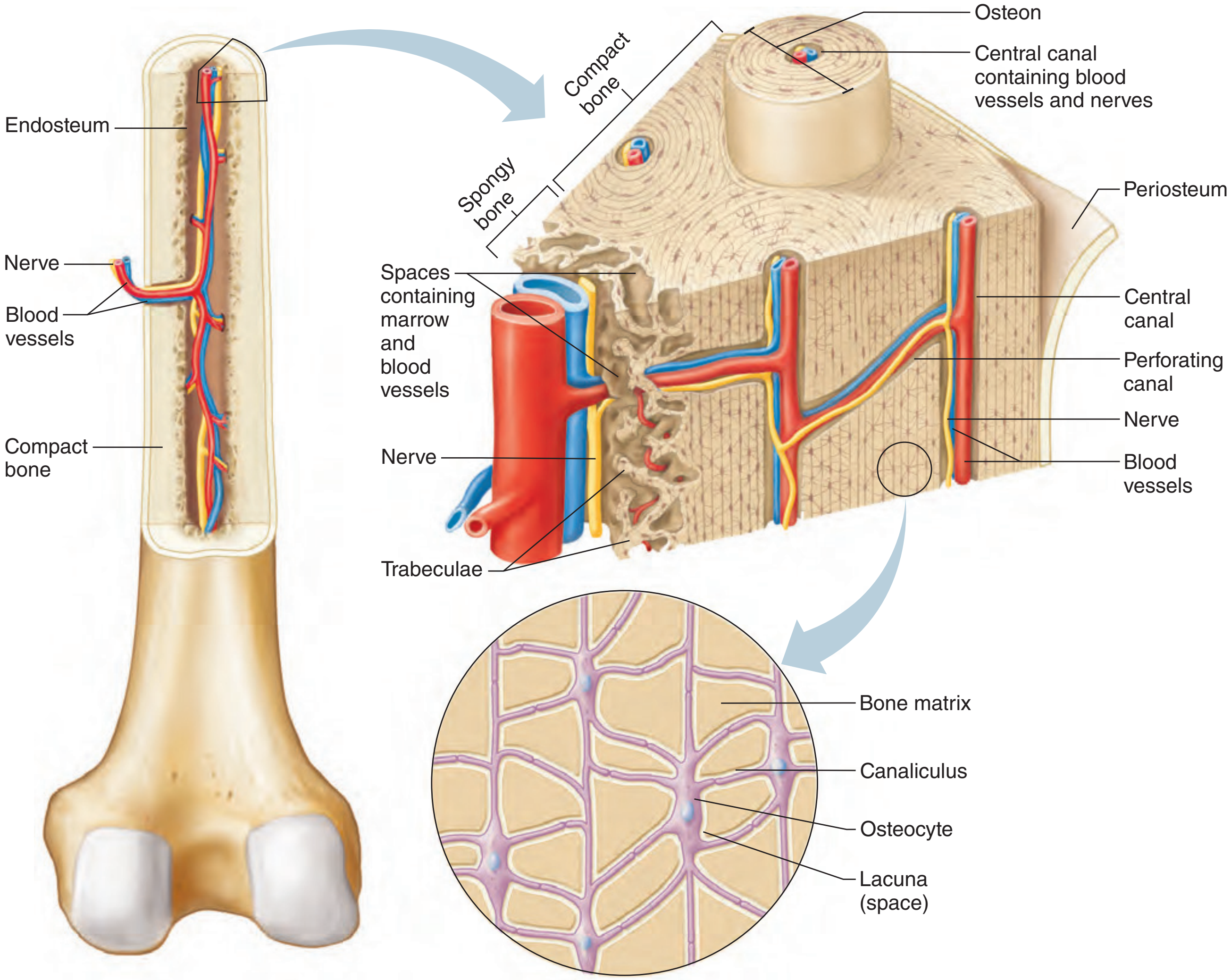

Endosteum
Nerve
Blood vessels
Compact bone
Compact bone
Spongy bone
Osteon
Central canal containing blood vessels and nerves
Periosteum
Spaces containing marrow and blood vessels
Nerve
Trabeculae
Central canal
Perforating canal
Nerve
Blood vessels
Bone matrix
Canaliculus
Osteocyte
Lacuna (space)

**FIGURE 7.3** APR Compact bone is composed of osteons cemented together by bone matrix. Extensions from osteocytes communicate through tunnel-like canaliculi. (Note: Drawings are not to scale.)

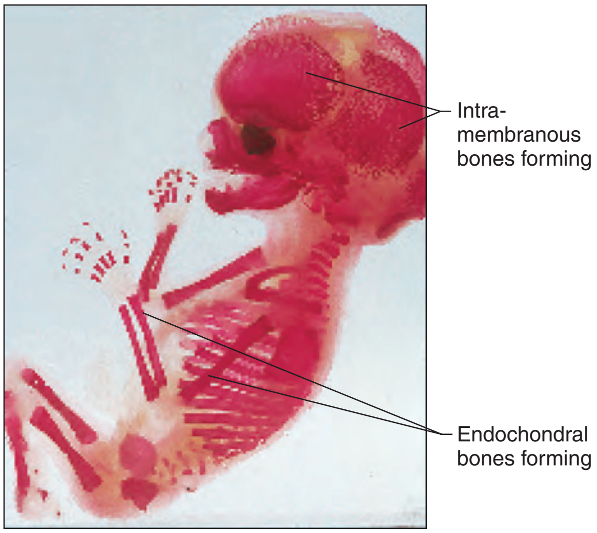

Intra-
membranous
bones forming
Endochondral
bones forming

**FIGURE 7.4** Intramembranous bones in the fetus form by replacing unspecialized connective tissue. Endochondral bones form from hyaline cartilage "models" that are gradually replaced with the harder tissue of bone. Note the stained, developing bones of this fourteen-week fetus.

## Intramembranous Bones

The flat bones of the skull are **intramembranous bones** (in″trah-mem′brah-nus bōnz). During their development, membranelike layers of unspecialized, or relatively undifferentiated, connective tissues appear at the sites of the future bones. Dense networks of blood vessels are contained within these connective tissues. Some of the partially differentiated progenitor cells enlarge and further differentiate into bone-forming cells called **osteoblasts** (os′te-o-blastz). The osteoblasts deposit bony matrix around themselves, forming spongy bone tissue in all directions within the layers of connective tissues. When extracellular matrix completely surrounds osteoblasts, they are called **osteocytes.** Eventually, cells of the membranous tissues that persist outside the developing bone give rise to the periosteum. Osteoblasts on the inside of the periosteum form a layer of compact bone over the surface of the newly formed spongy bone. The formation of bone is called **ossification** (os″ĭ-fi-ka′shun).

## Endochondral Bones

Most of the bones of the skeleton are **endochondral bones** (en″do-kon′dral bōnz). They develop in the fetus from masses of hyaline cartilage shaped like future bony structures. These cartilaginous models grow rapidly for a time and then begin to change extensively.

In a long bone, changes begin in the center of the diaphysis, where the cartilage slowly breaks down and disappears (fig. 7.5). At about the same time, a periosteum forms from connective tissue that encircles the developing diaphysis. Blood vessels and osteoblasts from the periosteum invade the disintegrating cartilage, and spongy bone forms in its place. This region of bone formation is called the *primary ossification center,* and bone tissue develops from it toward the ends of the cartilaginous structure. Meanwhile, osteoblasts from the periosteum deposit a thin layer of compact bone around the primary ossification center.

The epiphyses of the developing bone remain cartilaginous and continue to grow. Later, *secondary ossification centers* appear in the epiphyses, and spongy bone

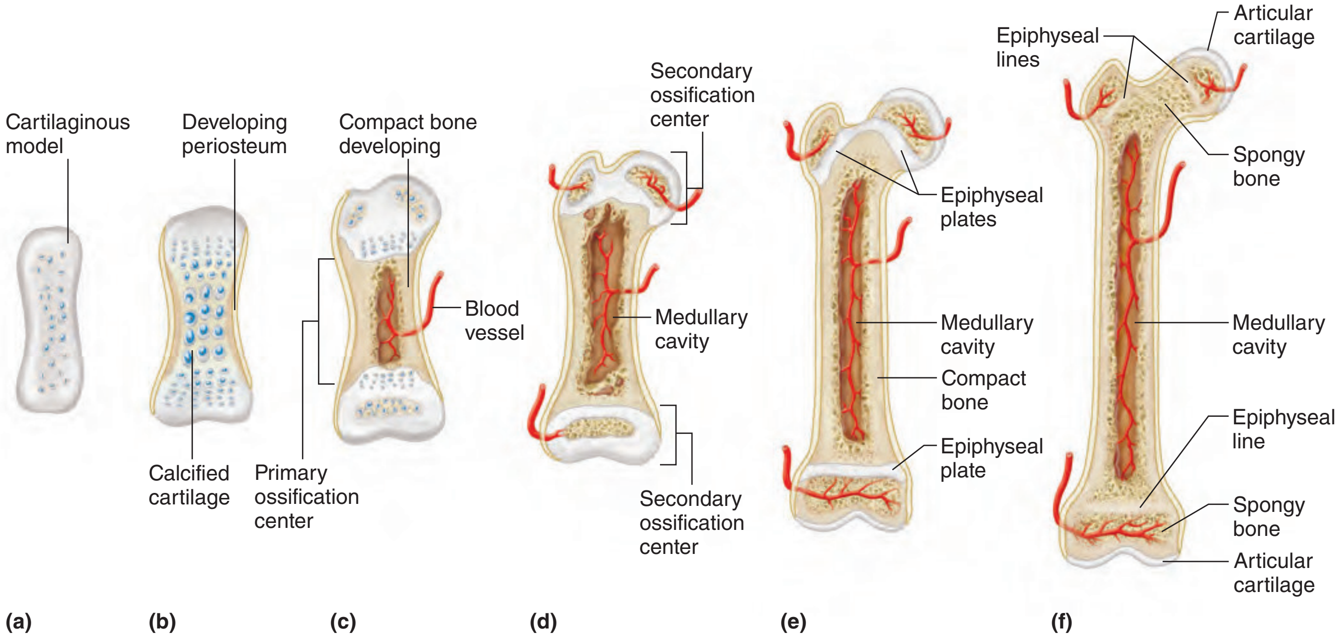

Cartilaginous
model
Developing
periosteum
Compact bone
developing
Secondary
ossification
center
Epiphyseal
lines
Articular
cartilage
Spongy
bone
Epiphyseal
plates
Blood
vessel
Medullary
cavity
Medullary
cavity
Medullary
cavity
Compact
bone
Epiphyseal
plate
Epiphyseal
line
Spongy
bone
Articular
cartilage
Calcified
cartilage
Primary
ossification
center
Secondary
ossification
center
(a)
(b)
(c)
(d)
(e)
(f)

**FIGURE 7.5** Major stages **(a–d** fetal, **e** child) in the development of an endochondral bone. In an **(f)** adult, when bone growth ceases, an epiphyseal line is what remains of the epiphyseal plate. (Relative bone sizes are not to scale.)

forms in all directions from them. As spongy bone is deposited in the diaphysis and in the epiphysis, a band of cartilage called the **epiphyseal plate** (ep″ĭ-fiz′e-al plāt) remains between these two ossification centers.

The cartilaginous tissue of the epiphyseal plate includes layers of young cells that are undergoing mitosis and producing new cells. As these cells enlarge and extracellular matrix forms around them, the cartilaginous plate thickens, lengthening the bone. At the same time, calcium salts accumulate in the extracellular matrix adjacent to the oldest cartilaginous cells, and as the extracellular matrix calcifies, the cells begin to die.

In time, large, multinucleated cells called **osteoclasts** (os′te-o-klastz) break down the calcified extracellular matrix. These large, multinucleated cells originate in bone marrow when certain single-nucleated white blood cells (monocytes) fuse. Osteoclasts secrete an acid that dissolves the inorganic component of the calcified matrix, and their lysosomal enzymes digest the organic components. After osteoclasts remove the extracellular matrix, bone-building osteoblasts invade the region and deposit new bone tissue in place of the calcified cartilage.

A long bone continues to lengthen while the cartilaginous cells of the epiphyseal plates are active (fig. 7.6). However, once the ossification centers of the diaphysis and epiphyses meet and the epiphyseal plates ossify, lengthening is no longer possible in that end of the bone.

A developing long bone thickens as compact bone is deposited on the outside, just beneath the periosteum. As this compact bone forms on the surface, osteoclasts erode other bone tissue on the inside. The resulting space becomes the medullary cavity of the diaphysis, which later fills with marrow. The bone in the central regions of the epiphyses and diaphysis remains spongy, and hyaline cartilage on the ends of the epiphyses persists throughout life as articular cartilage.

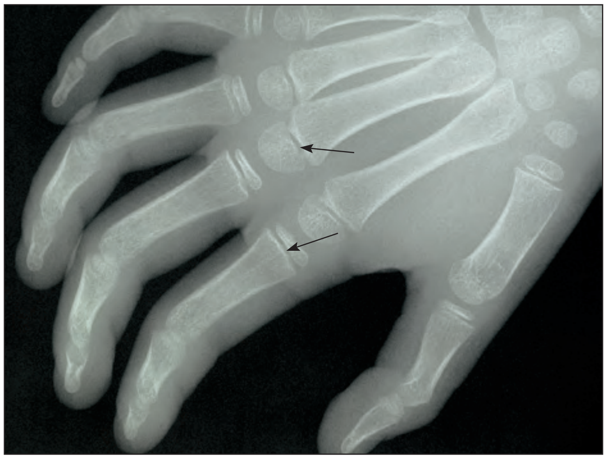


**FIGURE 7.6** APR Radiograph of the right hand. Epiphyseal plates (arrows) in a child's bones indicates that the bones are still lengthening.

If an epiphyseal plate is damaged as a result of a fracture before it ossifies, elongation of the long bone may prematurely cease, or if growth continues, it may be uneven. For this reason, injuries to the epiphyses of a young person's bones are of special concern. Surgery may be used on an epiphysis to equalize growth of bones developing at very different rates.

## Homeostasis of Bone Tissue

After the intramembranous and endochondral bones form, the actions of osteoclasts and osteoblasts continually remodel them. Throughout life, osteoclasts resorb bone matrix and osteoblasts replace it. Hormones that regulate blood calcium help control these opposing processes of *resorption* and *deposition* of matrix (see chapter 11, pp. 312–313). As a result, the total mass of bone tissue of an adult skeleton normally remains nearly constant, even though 3–5% of bone calcium is exchanged each year.

## Factors Affecting Bone Development, Growth, and Repair APR

A number of factors influence bone development, growth, and repair. These include nutrition, hormonal secretions, and physical exercise. For example, vitamin D is necessary for proper absorption of calcium in the small intestine. In the absence of this vitamin, dietary calcium is poorly absorbed, and the inorganic salt portion of bone matrix will lack calcium, softening and thereby deforming bones. Growth hormone secreted by the pituitary gland stimulates division of the cartilage cells in the epiphyseal plates. Sex hormones stimulate ossification of the epiphyseal plates. Physical exercise pulling on muscular attachments to bones stresses the bones, stimulating the bone tissue to thicken and strengthen. Clinical Application 7.1 describes repair of a fractured bone.

### PRACTICE

6. Describe the development of an intramembranous bone.
7. Explain how an endochondral bone develops.
8. Explain how osteoclasts and osteoblasts remodel bone.
9. Explain how nutritional factors, hormones, and physical exercise affect bone development and growth.

## 7.4 | Bone Function

Bones shape, support, and protect body structures. They also aid body movements, house tissue that produces blood cells, and store inorganic salts.

## Support and Protection

Bones give shape to structures such as the head, face, thorax, and limbs. They also provide support and protection. For example, the bones of the lower limbs, pelvis, and backbone support the body's weight. The bones of the skull protect the eyes, ears, and brain. Bones of the rib cage and shoulder girdle protect the heart and lungs, whereas the bones of the pelvic girdle protect the lower abdominal and internal reproductive organs.

## Body Movement

Whenever limbs or other body parts move, bones and muscles interact as simple mechanical devices called **levers** (lev′erz). A lever has four basic components: (1) a rigid bar or rod, (2) a fulcrum or pivot on which the bar turns, (3) an object moved against resistance, and (4) a force that supplies energy for the movement of the bar.

The actions of bending and straightening the upper limb at the elbow illustrate bones and muscles functioning as levers. When the upper limb bends, the forearm bones represent the rigid bar, the elbow joint is the fulcrum, the hand is moved against the resistance provided by the weight, and the force is supplied by muscles on the anterior side of the arm (fig. 7.7*a*). One of these muscles, the *biceps brachii,* is attached by a tendon to a projection on a bone (radius) in the forearm, a short distance distal to the elbow.

When the upper limb straightens at the elbow, the forearm bones again serve as the rigid bar, the elbow joint serves as the fulcrum, and the hand moves against the resistance by pulling on the rope to raise the weight (fig. 7.7*b*). However, in this case the *triceps brachii,* a muscle located on the posterior side of the arm, supplies the force. A tendon of this muscle attaches to a projection on a forearm bone (ulna) at the point of the elbow.

## Blood Cell Formation

The process of blood cell formation, called **hematopoiesis** (he″mă-to-poi-e′sis), begins in the *yolk sac,* which lies outside the human embryo (see chapter 20, p. 557). Later in development, blood cells are manufactured in the liver and spleen, and still later they form in bone marrow.

Marrow is a soft, netlike mass of connective tissue within the medullary cavities of long bones, in the irregular spaces of spongy bone, and in the larger central canals of compact bone tissue. It is of two kinds: red and yellow. *Red marrow* functions in the formation of red blood cells (erythrocytes), white blood cells (leukocytes), and blood platelets. The color comes from the oxygen-carrying pigment **hemoglobin** in the red blood cells.

In an infant, red marrow occupies the cavities of most bones. With increasing age, yellow marrow replaces much of it. *Yellow marrow* stores fat; it is not active in blood cell production. In an adult, red marrow is primarily found in the spongy bone of the skull, ribs, sternum, clavicles, vertebrae, and hip bones. If the supply of blood cells is deficient, some yellow marrow may become red marrow, which then reverts to yellow marrow when the deficiency is corrected. Chapter 12 (pp. 329, 334, and 336) describes blood cell formation in more detail.

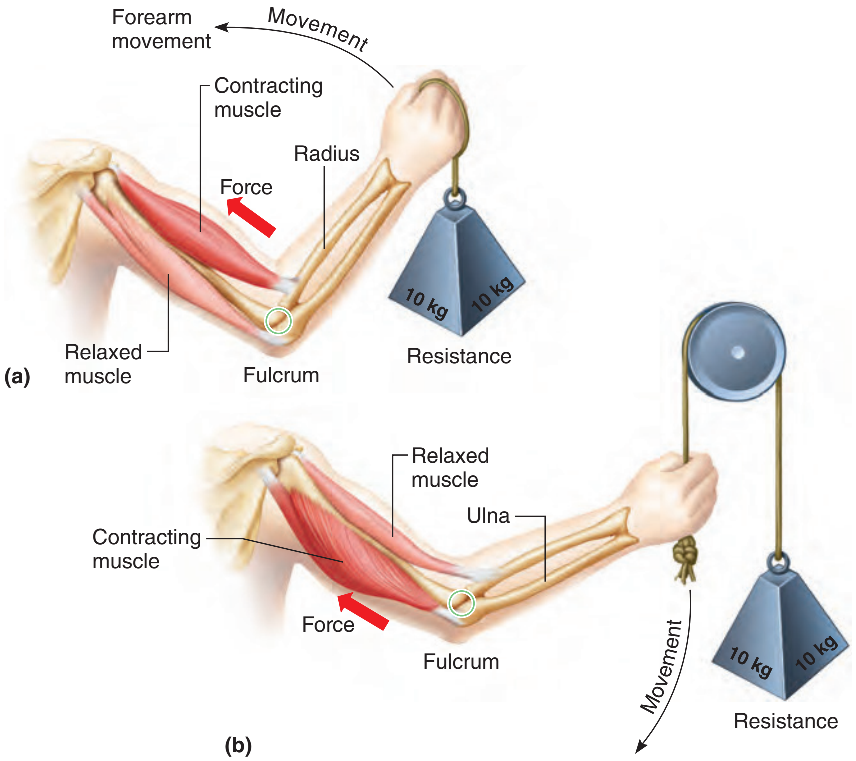


**FIGURE 7.7** Levers and movement. **(a)** When the forearm bends at the elbow or **(b)** when the forearm straightens at the elbow, the bones and muscles function as a lever.

## CLINICAL APPLICATION 7.1

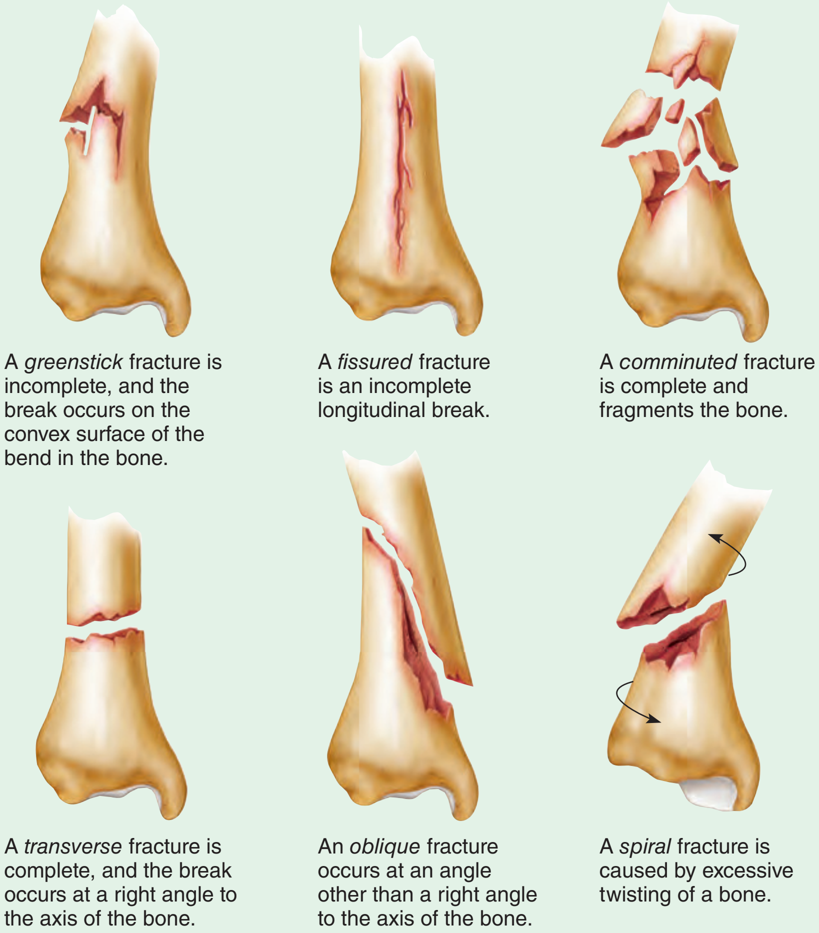
## Bone Fractures

A *fracture* is a break in a bone. A fracture is classified by its cause as a traumatic, spontaneous, or pathologic fracture and by the nature of the break as a greenstick, fissured, comminuted, transverse, oblique, or spiral fracture (fig. 7A). A broken bone exposed to the outside by an opening in the skin is termed a compound (open) fracture.

When a bone breaks, blood vessels in it rupture, and the periosteum is likely to tear. Blood from the broken vessels spreads through the damaged area and soon forms a blood clot, or *hematoma.* Vessels in surrounding tissues dilate, swelling and inflaming the tissues.

Within days or weeks, developing blood vessels and large numbers of osteoblasts originating in the periosteum invade the hematoma. The osteoblasts rapidly divide in the regions close to the new blood vessels, building spongy bone nearby. Granulation tissue develops, and in regions farther from a blood supply, fibroblasts produce masses of fibrocartilage. Meanwhile, phagocytic cells begin to remove the blood clot, as well as any dead or damaged cells in the affected area. Osteoclasts also appear and resorb bone fragments, aiding in "cleaning up" debris.

In time, fibrocartilage fills the gap between the ends of the broken bone. This mass, a *cartilaginous soft callus,* is later


A *greenstick* fracture is incomplete, and the break occurs on the convex surface of the bend in the bone.

A *fissured* fracture is an incomplete longitudinal break.

A *comminuted* fracture is complete and fragments the bone.

A *transverse* fracture is complete, and the break occurs at a right angle to the axis of the bone.

An *oblique* fracture occurs at an angle other than a right angle to the axis of the bone.

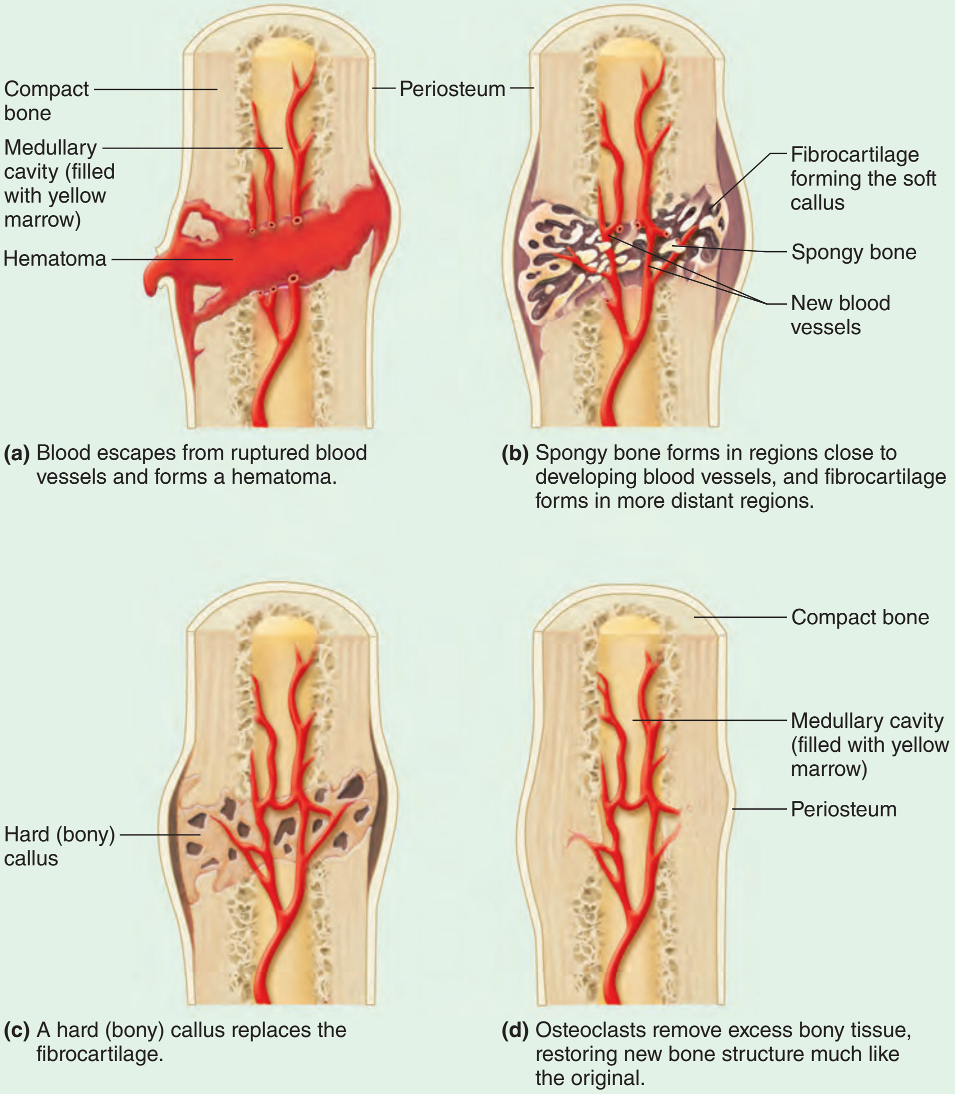
A *spiral* fracture is caused by excessive twisting of a bone.

**FIGURE 7A** Various types of fractures.

replaced by bone tissue in much the same way that the hyaline cartilage of a developing endochondral bone is replaced. That is, the cartilaginous callus breaks down, blood vessels and osteoblasts invade the area, and a *hard bony callus* fills the space.

Typically, more bone is produced at the site of a healing fracture than is necessary to replace the damaged tissues. Osteoclasts remove the excess, and the result is a bone shaped much like the original (fig. 7B).

Several techniques are used to help the bone-healing process. The first casts to immobilize fractured bones were introduced in 1876, and soon after, doctors began using screws and plates internally to align healing bone parts. Today, orthopedic surgeons also use rods, wires, and nails. These devices have become lighter and smaller; many are built of titanium. A device called a hybrid fixator treats a broken leg using metal pins internally to align bone pieces. The pins are anchored to a metal ring device worn outside the leg. Experimental approaches to helping bones heal include cartilage grafts and infusions of stem cells taken from a patient's own bone marrow.


Compact bone
Medullary cavity (filled with yellow marrow)
Hematoma
Periosteum
Fibrocartilage forming the soft callus
Spongy bone
New blood vessels
Hard (bony) callus
Compact bone
Medullary cavity (filled with yellow marrow)
Periosteum

**(a)** Blood escapes from ruptured blood vessels and forms a hematoma.

**(b)** Spongy bone forms in regions close to developing blood vessels, and fibrocartilage forms in more distant regions.

**(c)** A hard (bony) callus replaces the fibrocartilage.

**(d)** Osteoclasts remove excess bony tissue, restoring new bone structure much like the original.

**FIGURE 7B** Major steps **(a–d)** in repair of a fracture.

Bone marrow transplants have been used for more than half a century to enable people with certain cancers to tolerate high levels of chemotherapy drugs. Replacing bone marrow is also a way to treat an inherited disorder of blood cells (such as sickle cell disease) or a disease of the descendants of these cells that function outside the circulation (such as the brain disease adrenoleukodystrophy).

In a bone marrow transplant, a hollow needle and syringe remove normal red marrow cells from the spongy bone of a donor, or stem cells (which can give rise to specialized blood cells) are separated out from the donor's bloodstream. Stem cells from the umbilical cord of a newborn can be used in place of bone marrow.

Donors are selected based on their cells having a pattern of molecules on their surfaces that closely matches that of the recipient's cells. In 30% of bone marrow transplants from donors, the donor is a blood relative. The cells are injected into the bloodstream of the recipient, whose own marrow has been intentionally destroyed with radiation or chemotherapy. If all goes well, the donor cells travel to the spaces within bones that red marrow normally occupies, where they replenish the blood supply with healthy cells. About 15% of the time, patients die from infection because their immune systems reject the transplant, or because the transplanted tissue attacks the recipient, a condition called graft-versus-host disease.

Safer than a bone marrow transplant for some conditions is an autologous ("self") stem cell transplant. Stem cells are taken from a patient's bloodstream, and a mutation corrected or healthy cells separated and cultured. Or the bone marrow is stimulated to make stem cells, which are isolated and reintroduced into the patient. Then high doses of chemotherapy or radiation are used to destroy the rest of the bone marrow in the patient's body, and the patient's stem cells are infused. They migrate to the bone marrow and reconstitute a disease-free blood-forming system that the patient's immune system does not reject.

## Storage of Inorganic Salts

Bones store calcium. The extracellular matrix of bone tissue is rich in calcium salts, mostly in the form of calcium phosphate. Vital metabolic processes require calcium. When the blood is low in calcium, parathyroid hormone stimulates osteoclasts to break down bone tissue, releasing calcium salts from the extracellular matrix into the blood. A high blood calcium level inhibits osteoclast activity, and calcitonin from the thyroid gland stimulates osteoblasts to form bone tissue, storing excess calcium in the extracellular matrix (fig. 7.8). Chapter 11 (pp. 312–313) describes the details of this homeostatic mechanism. Maintaining sufficient blood calcium levels is important in muscle contraction, nerve cell function, blood clotting, and other physiological processes.

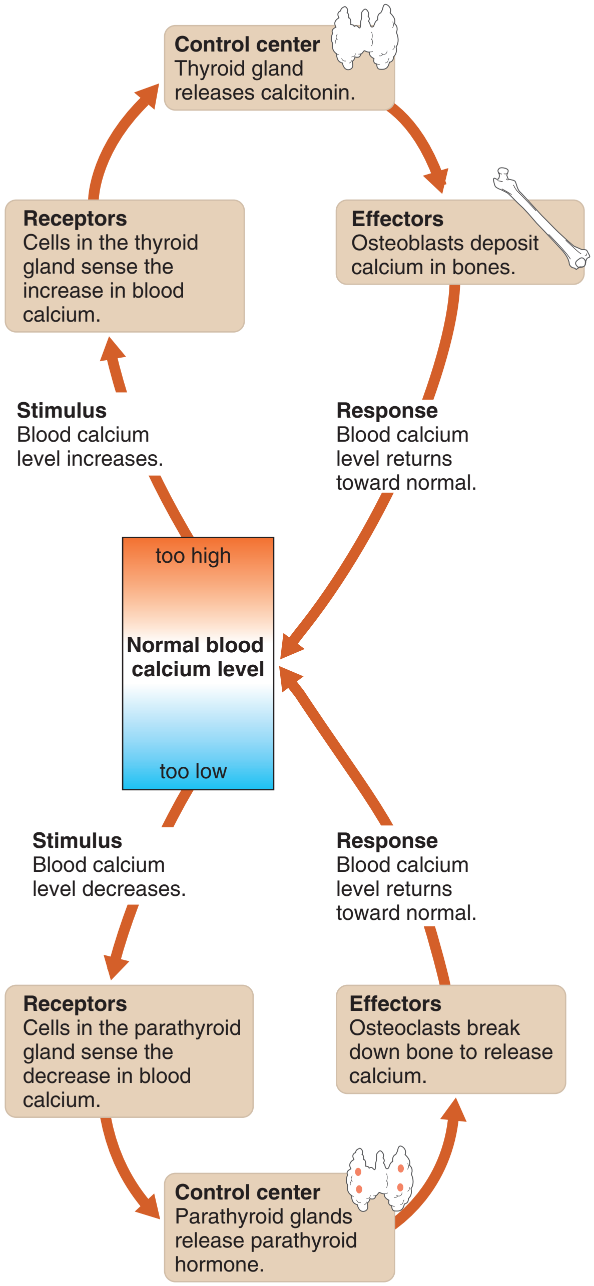

Control center
Thyroid gland releases calcitonin.
Receptors
Cells in the thyroid gland sense the increase in blood calcium.
Effectors
Osteoblasts deposit calcium in bones.
Stimulus
Blood calcium level increases.
Response
Blood calcium level returns toward normal.
too high
Normal blood calcium level
too low
Stimulus
Blood calcium level decreases.
Response
Blood calcium level returns toward normal.
Receptors
Cells in the parathyroid gland sense the decrease in blood calcium.
Effectors
Osteoclasts break down bone to release calcium.
Control center
Parathyroid glands release parathyroid hormone.

**FIGURE 7.8** APR Hormonal regulation of bone calcium deposition and resorption.

Q *What three components of a homeostatic mechanism (see fig. 1.5, p. 14) are shown in this figure?*

**Answer can be found in Appendix F on page 582.**

In addition to storing calcium and phosphorus, bone tissue contains smaller amounts of magnesium, sodium, potassium, and carbonate ions. Bones also accumulate certain harmful metallic elements such as lead, radium, or strontium, which are not normally present in the body but are sometimes accidentally ingested.

## PRACTICE

10. Name the major functions of bones.
11. Distinguish between the functions of red marrow and yellow marrow.
12. List the substances normally stored in bone tissue.

## 7.5 | Skeletal Organization

For purposes of study, it is convenient to divide the skeleton into two major portions—an axial skeleton and an appendicular skeleton (fig. 7.9). The **axial skeleton** consists of the bony and cartilaginous parts that support and protect the organs of the head, neck, and trunk. These parts include:

1. **Skull.** The skull is composed of the **cranium** (kra′ne-um), or brain case, and the *facial bones.*
2. **Hyoid bone.** The hyoid (hi′oid) bone is located in the neck between the lower jaw and the larynx. It supports the tongue and is an attachment for certain muscles that help move the tongue during swallowing.
3. **Vertebral column.** The vertebral column, or spinal column (backbone), consists of many vertebrae separated by cartilaginous *intervertebral discs.* Near its distal end, five vertebrae fuse to form the **sacrum** (sa′krum), part of the pelvis. The

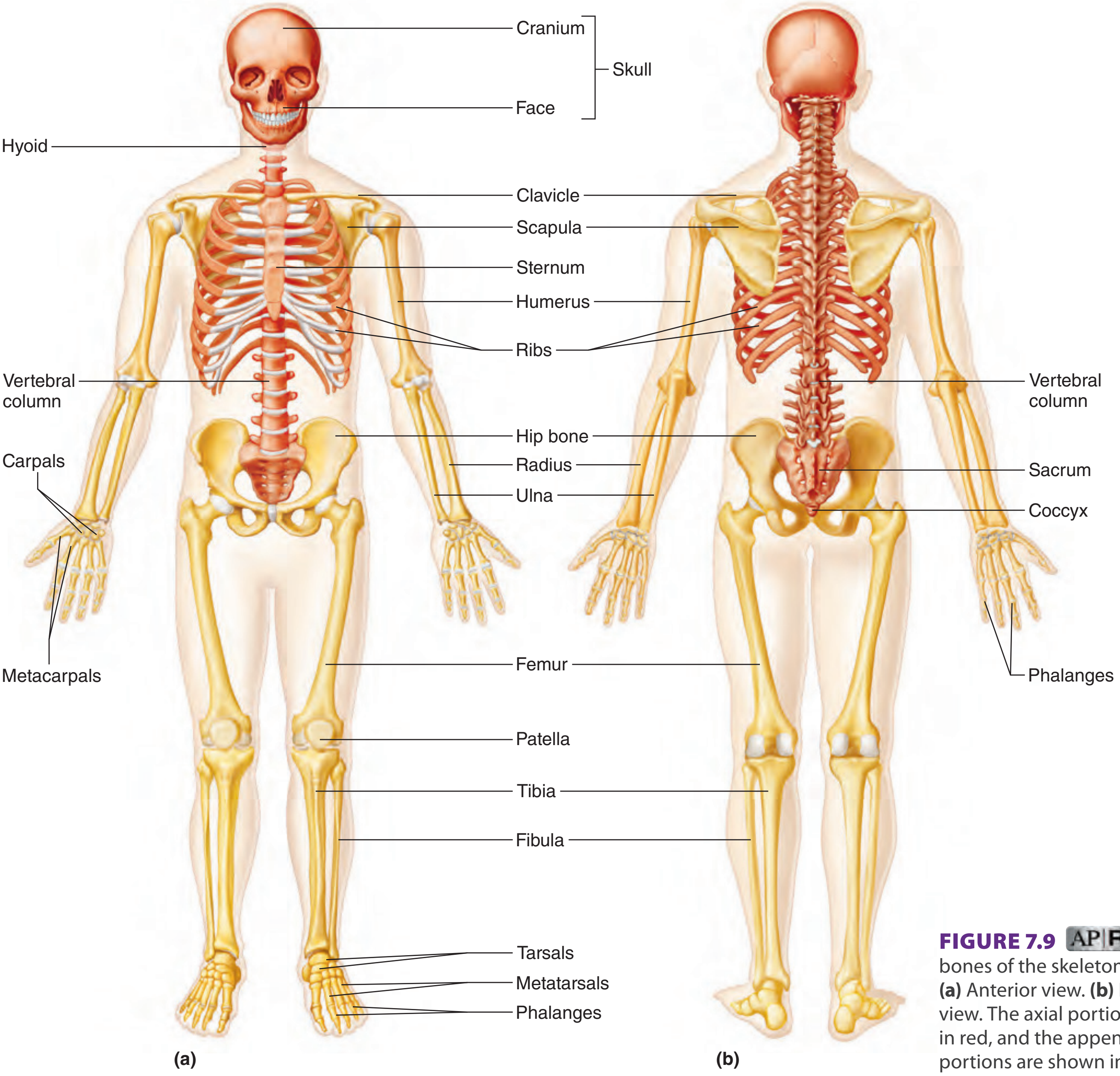

Cranium
Skull
Face
Hyoid
Clavicle
Scapula
Sternum
Humerus
Ribs
Vertebral column
Carpals
Hip bone
Radius
Ulna
Metacarpals
Femur
Patella
Tibia
Fibula
Tarsals
Metatarsals
Phalanges
Vertebral column
Sacrum
Coccyx
Phalanges
(a)
(b)

**FIGURE 7.9** APR Major bones of the skeleton. **(a)** Anterior view. **(b)** Posterior view. The axial portion is shown in red, and the appendicular portions are shown in yellow.

**coccyx** (kok′siks), a small, rudimentary tailbone composed of four fused vertebrae, is attached to the end of the sacrum.

4. **Thoracic cage.** The thoracic cage protects the organs of the thoracic cavity and the upper abdominal cavity. It is composed of twelve pairs of **ribs,** which articulate posteriorly with thoracic vertebrae. The thoracic cage also includes the **sternum** (ster′num), or breastbone, to which most of the ribs attach anteriorly.

The **appendicular skeleton** consists of the bones of the upper and lower limbs and the bones that anchor the limbs to the axial skeleton. It includes:

1. **Pectoral girdle.** The pectoral (pek′to-ral) girdle is formed by a **scapula** (scap′u-lah), or shoulder blade, and a **clavicle** (klav′ĭ-k′l), or collarbone, on both sides of the body. The pectoral girdle connects the bones of the upper limbs to the axial skeleton and aids in upper limb movements.
2. **Upper limbs.** Each upper limb consists of a **humerus** (hu′mer-us), or arm bone, two forearm bones—a **radius** (ra′de-us) and an **ulna** (ul′nah)—and a hand. The humerus, radius, and ulna articulate with each other at the elbow joint. At the distal end of the radius and ulna is the hand. There are eight **carpals** (kar′pals), or wrist bones. The five bones of the palm are called **metacarpals** (met″ah-kar′pals), and the fourteen finger bones are called **phalanges** (fah-lan′jēz; singular, *phalanx,* fa′lanks).
3. **Pelvic girdle.** The pelvic girdle is formed by two hip bones attached to each other anteriorly and to the sacrum posteriorly. They connect the bones of the lower limbs to the axial skeleton and, with the sacrum and coccyx, form the **pelvis.**
4. **Lower limbs.** Each lower limb consists of a **femur** (fe′mur), or thigh bone, two leg bones—a large **tibia** (tib′e-ah) and a slender **fibula** (fib′u-lah)—and a foot. The femur and tibia articulate with each other at the knee joint, where the **patella** (pah-tel′ah) covers the anterior surface. At the distal ends of the tibia and fibula is the foot. There are seven **tarsals** (tahr′sals), or ankle bones. The five bones of the instep are called **metatarsals** (met″ah-tahr′sals), and the fourteen bones of the toes (like the fingers) are called **phalanges.**

Table 7.1 lists the bones of the adult skeleton. Table 7.2 lists terms that describe skeletal structures.

**TABLE 7.1** **Bones of the Adult Skeleton**

| | | |
|---|---|---|
| 1. Axial Skeleton | | |
| a. Skull | | |
| 8 cranial bones | | |
| frontal 1 | temporal 2 | |
| parietal 2 | sphenoid 1 | |
| occipital 1 | ethmoid 1 | |
| 14 facial bones | | |
| maxilla 2 | lacrimal 2 | |
| zygomatic 2 | nasal 2 | |
| palatine 2 | vomer 1 | |
| inferior nasal concha 2 | | |
| mandible 1 | | 22 bones |
| b. Middle ear bones | | |
| malleus 2 | | |
| incus 2 | | |
| stapes 2 | | 6 bones |
| c. Hyoid | | |
| hyoid bone 1 | | 1 bone |
| d. Vertebral column | | |
| cervical vertebra 7 | | |
| thoracic vertebra 12 | | |
| lumbar vertebra 5 | | |
| sacrum 1 | | |
| coccyx 1 | | 26 bones |
| e. Thoracic cage | | |
| rib 24 | | |
| sternum 1 | | 25 bones |
| 2. Appendicular Skeleton | | |
| a. Pectoral girdle | | |
| scapula 2 | | |
| clavicle 2 | | 4 bones |
| b. Upper limbs | | |
| humerus 2 | | |
| radius 2 | | |
| ulna 2 | | |
| carpal 16 | | |
| metacarpal 10 | | |
| phalanx 28 | | 60 bones |
| c. Pelvic girdle | | |
| hip bone 2 | | 2 bones |
| d. Lower limbs | | |
| femur 2 | | |
| tibia 2 | | |
| fibula 2 | | |
| patella 2 | | |
| tarsal 14 | | |
| metatarsal 10 | | |
| phalanx 28 | | 60 bones |
| | Total | 206 bones |

## TABLE 7.2 Terms Used to Describe Skeletal Structures

| Term | Definition | Examples |
|---|---|---|
| Condyle (kon′dīl) | Rounded process that usually articulates with another bone | Occipital condyle of the occipital bone (fig. 7.13) |
| Crest (krest) | Narrow, ridgelike projection | Iliac crest of the ilium (fig. 7.28) |
| Epicondyle (ep″ĭ-kon′dīl) | Projection situated above a condyle | Medial epicondyle of the humerus (fig. 7.24) |
| Facet (fas′et) | Small, nearly flat surface | Rib facet of the thoracic vertebra (fig. 7.17) |
| Fontanel (fon″tah-nel′) | Soft spot in the skull where membranes cover the space between bones | Anterior fontanel between the frontal and parietal bones (fig. 7.16) |
| Foramen (fo-ra′men) | Opening through a bone that usually is a passageway for blood vessels, nerves, or ligaments | Foramen magnum of the occipital bone (fig. 7.13) |
| Fossa (fos′ah) | Relatively deep pit or depression | Olecranon fossa of the humerus (fig. 7.24) |
| Fovea (fo′ve-ah) | Tiny pit or depression | Fovea capitis of the femur (fig. 7.30) |
| Head (hed) | Enlargement on the end of a bone | Head of the humerus (fig. 7.24) |
| Meatus (me-a′tus) | Tubelike passageway within a bone | External acoustic meatus of the temporal bone (fig. 7.12) |
| Process (pros′es) | Prominent projection on a bone | Mastoid process of the temporal bone (fig. 7.12) |
| Sinus (si′nus) | Cavity within a bone | Frontal sinus of the frontal bone (fig. 7.15) |
| Spine (spīn) | Thornlike projection | Spine of the scapula (fig. 7.23) |
| Sulcus (sul′kus) | Furrow or groove | Intertubercular sulcus of the humerus (fig. 7.24) |
| Suture (soo′cher) | Interlocking line of union between bones | Lambdoid suture between the occipital and parietal bones (fig. 7.12) |
| Trochanter (tro-kan′ter) | Relatively large process | Greater trochanter of the femur (fig. 7.30) |
| Tubercle (tu′ber-kl) | Small, knoblike process | Greater tubercle of the humerus (fig. 7.24) |
| Tuberosity (tu″bĕ-ros′ĭ-te) | Knoblike process usually larger than a tubercle | Radial tuberosity of the radius (fig. 7.25) |

**FACTS OF LIFE** The skeleton of an average 160-pound body weighs about 29 pounds.

**PRACTICE**

13. Distinguish between the axial and appendicular skeletons.
14. List the bones of the axial skeleton and of the appendicular skeleton.

## 7.6 | Skull APR

A human skull usually consists of twenty-two bones that, except for the lower jaw, are firmly interlocked along immoveable joints called *sutures* (soo′cherz) (fig. 7.10). Eight of these interlocked bones make up the cranium, and fourteen form the facial skeleton. (Three other bones in each middle ear are discussed in chapter 10, pp. 282–283.) Reference plates 8–11, on pages 185–187, show the human skull and its parts.

### Cranium

The **cranium** encloses and protects the brain, and its surface provides attachments for muscles that make chewing and head movements possible. Some of the cranial bones contain air-filled cavities called *paranasal sinuses,* lined with mucous membranes and connected by passageways to the nasal cavity (fig. 7.11). Sinuses reduce the skull's weight and increase the intensity of the voice by serving as resonant sound chambers.

The eight bones of the cranium, shown in figures 7.10 and 7.12, are:

1. **Frontal bone.** The frontal (frun′tal) bone forms the anterior portion of the skull above the eyes. On the upper margin of each orbit (the bony socket of the eye), the frontal bone is marked by a *supraorbital foramen* (or *supraorbital notch* in some skulls), through which blood vessels and nerves pass to the tissues of the forehead. Within the frontal bone are two *frontal sinuses,* one above each eye near the midline (see fig. 7.11).
2. **Parietal bones.** One parietal (pah-ri′ĕ-tal) bone is located on each side of the skull just behind the frontal bone (fig. 7.12). Together, the parietal bones

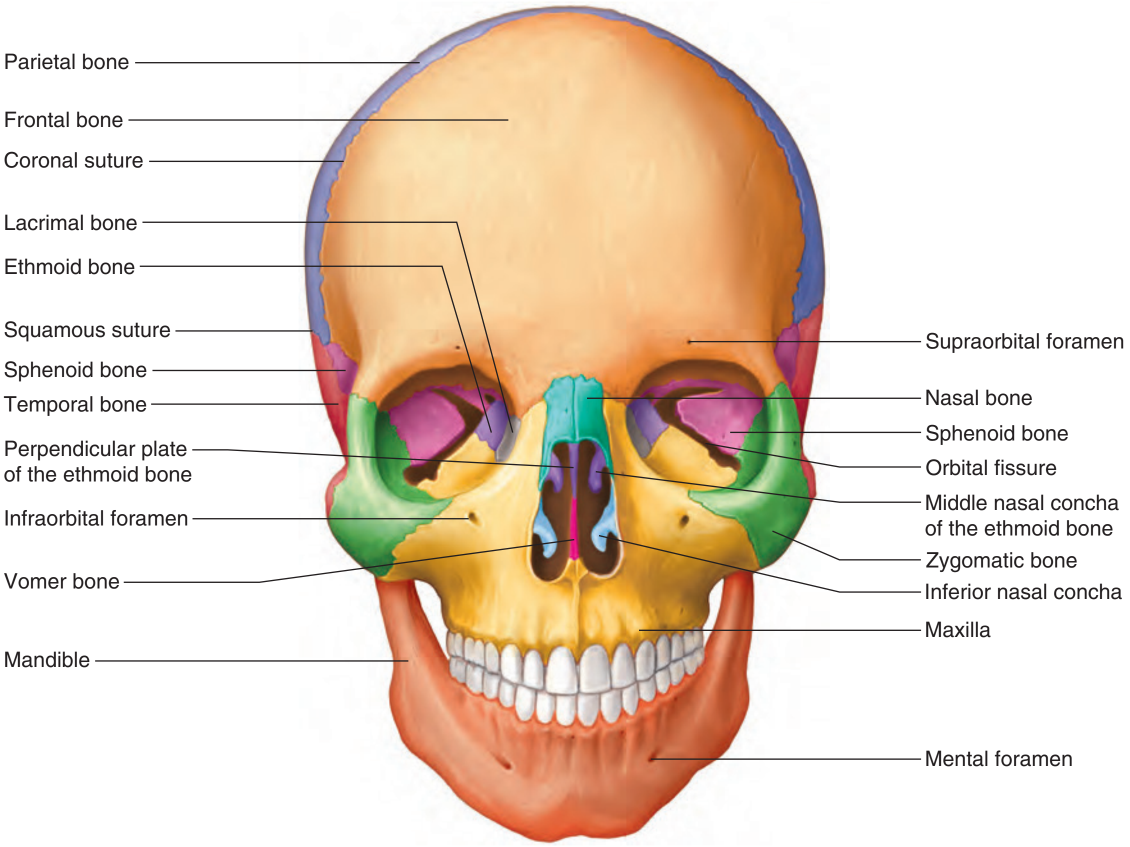

Parietal bone
Frontal bone
Coronal suture
Lacrimal bone
Ethmoid bone
Squamous suture
Sphenoid bone
Temporal bone
Perpendicular plate of the ethmoid bone
Infraorbital foramen
Vomer bone
Mandible
Supraorbital foramen
Nasal bone
Sphenoid bone
Orbital fissure
Middle nasal concha of the ethmoid bone
Zygomatic bone
Inferior nasal concha
Maxilla
Mental foramen

**FIGURE 7.10** APR Anterior view of the skull.

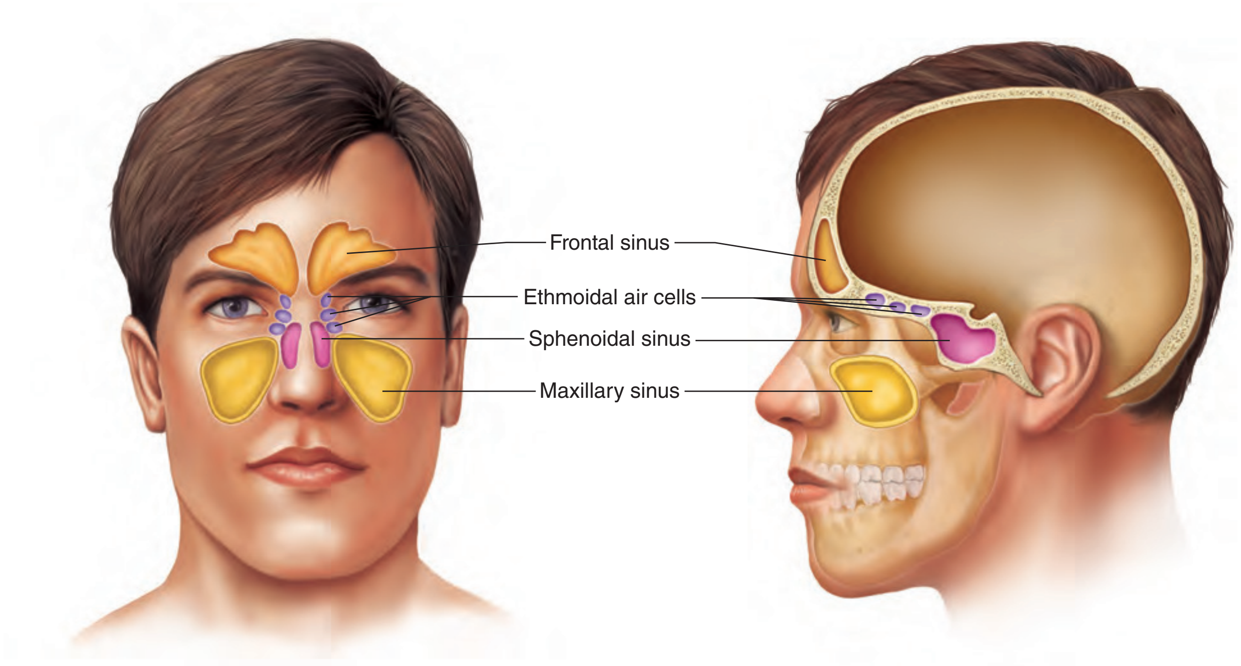

Frontal sinus
Ethmoidal air cells
Sphenoidal sinus
Maxillary sinus

**FIGURE 7.11** Locations of the paranasal sinuses.

form the bulging sides and roof of the cranium. They are fused at the midline along the *sagittal suture,* and they meet the frontal bone along the *coronal suture.*

3. **Occipital bone.** The occipital (ok-sip′ĭ-tal) bone joins the parietal bones along the *lambdoid* (lam′doid) *suture* (figs. 7.12 and 7.13). It forms the back of the skull and the base of the cranium. A large opening on its lower surface is the *foramen magnum*, where nerve fibers from the brain enter the vertebral canal to become part of the spinal cord. Rounded processes called *occipital condyles,* located on each side of the foramen magnum, articulate with the first vertebra (atlas) of the vertebral column.
4. **Temporal bones.** A temporal (tem′po-ral) bone on each side of the skull joins the parietal bone along a *squamous suture* (see figs. 7.10 and 7.12). The temporal bones form parts of the sides and the base of the cranium. Located near the inferior margin is an opening, the *external acoustic meatus,* which leads inward to parts of the ear. The temporal bones have depressions called the *mandibular fossae* that articulate with condyles of the mandible. Below each external acoustic meatus are two projections—a rounded *mastoid process* and a long, pointed *styloid process.* The mastoid process provides an attachment for certain muscles of the neck, whereas the styloid process anchors muscles associated with the tongue and pharynx.

   A *zygomatic process* projects anteriorly from the temporal bone, joins the *zygomatic bone,* and helps form the prominence of the cheek.
5. **Sphenoid bone.** The sphenoid (sfe′noid) bone is wedged between several other bones in the anterior portion of the cranium (figs. 7.12 and 7.13). This bone helps form the base of the cranium, the sides of the skull, and the floors and sides of the orbits. Along the midline within the cranial cavity, a portion of the sphenoid bone indents to form the saddle-shaped *sella turcica* (sel′ah tur′si-ka). The pituitary gland occupies this depression. The sphenoid bone also contains two *sphenoidal sinuses* (see fig. 7.11).
6. **Ethmoid bone.** The ethmoid (eth′moid) bone is located in front of the sphenoid bone (figs. 7.12 and 7.14). It consists of two masses, one on each side of the nasal cavity, which are joined horizontally by thin *cribriform* (krib′rĭ-form) *plates.* These plates form part of the roof of the nasal cavity (fig. 7.14).

   Projecting upward into the cranial cavity between the cribriform plates is a triangular process of the ethmoid bone called the *crista galli* (kris′tă gal′li) (cock's comb). Membranes that enclose the brain attach to this process (figs. 7.14 and 7.15). Portions of the ethmoid bone also form sections of the cranial floor, the orbital walls, and the nasal cavity walls. A *perpendicular plate* projects downward in the

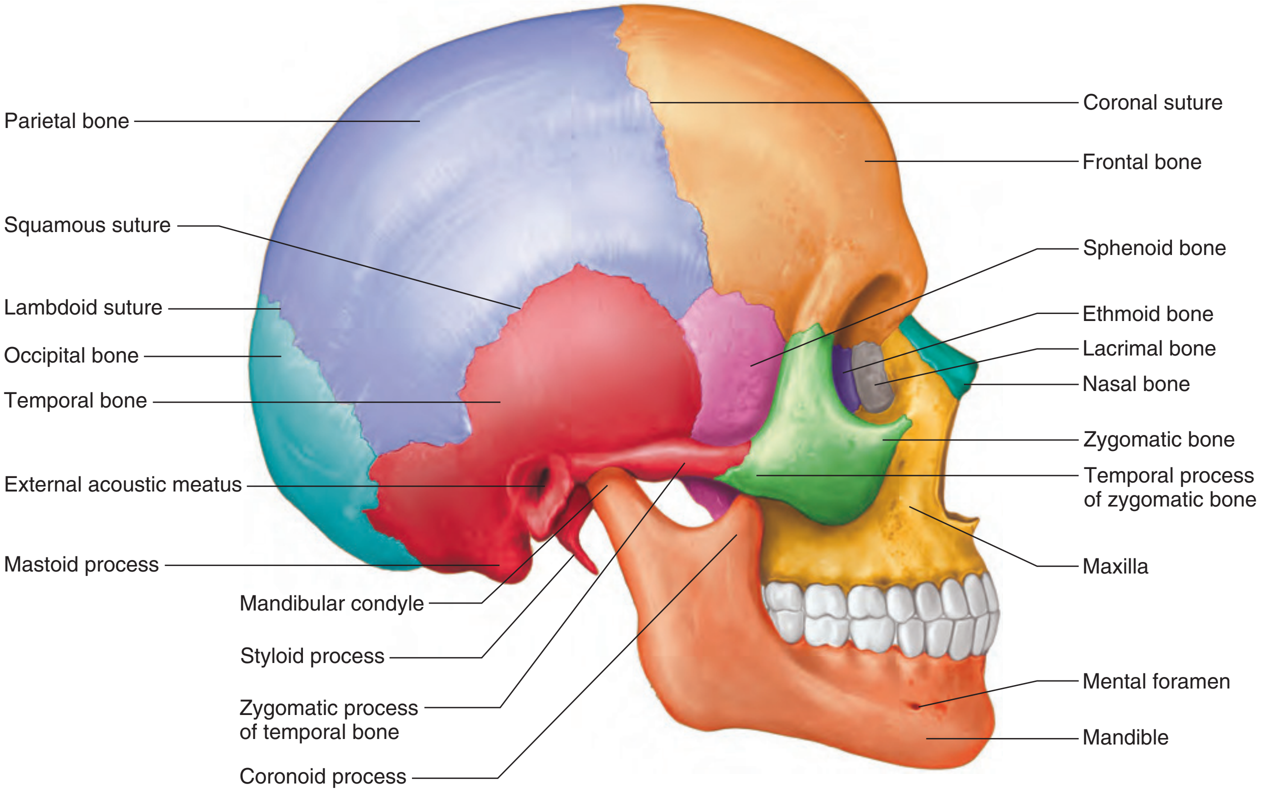

Parietal bone
Squamous suture
Lambdoid suture
Occipital bone
Temporal bone
External acoustic meatus
Mastoid process
Mandibular condyle
Styloid process
Zygomatic process of temporal bone
Coronoid process
Coronal suture
Frontal bone
Sphenoid bone
Ethmoid bone
Lacrimal bone
Nasal bone
Zygomatic bone
Temporal process of zygomatic bone
Maxilla
Mental foramen
Mandible

**FIGURE 7.12** APR Right lateral view of the skull.

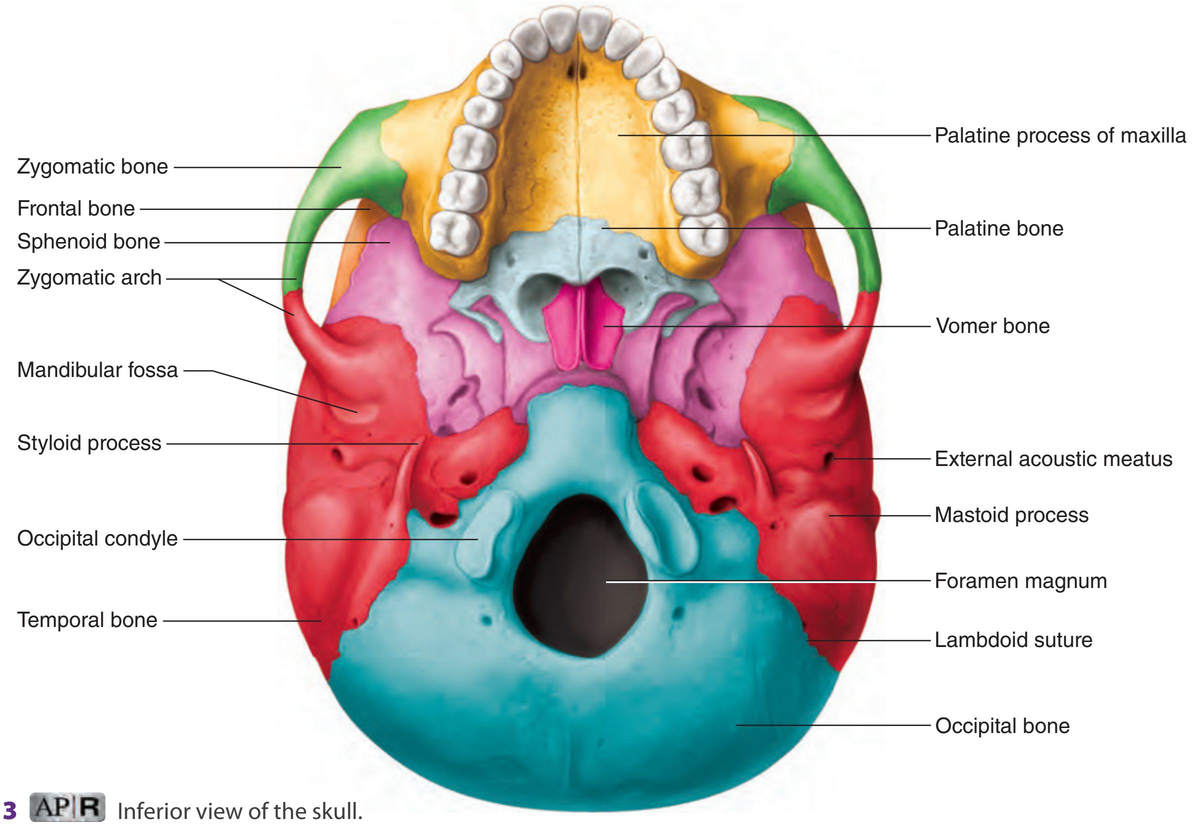

Zygomatic bone
Frontal bone
Sphenoid bone
Zygomatic arch
Mandibular fossa
Styloid process
Occipital condyle
Temporal bone
Palatine process of maxilla
Palatine bone
Vomer bone
External acoustic meatus
Mastoid process
Foramen magnum
Lambdoid suture
Occipital bone

**FIGURE 7.13** APIR Inferior view of the skull.

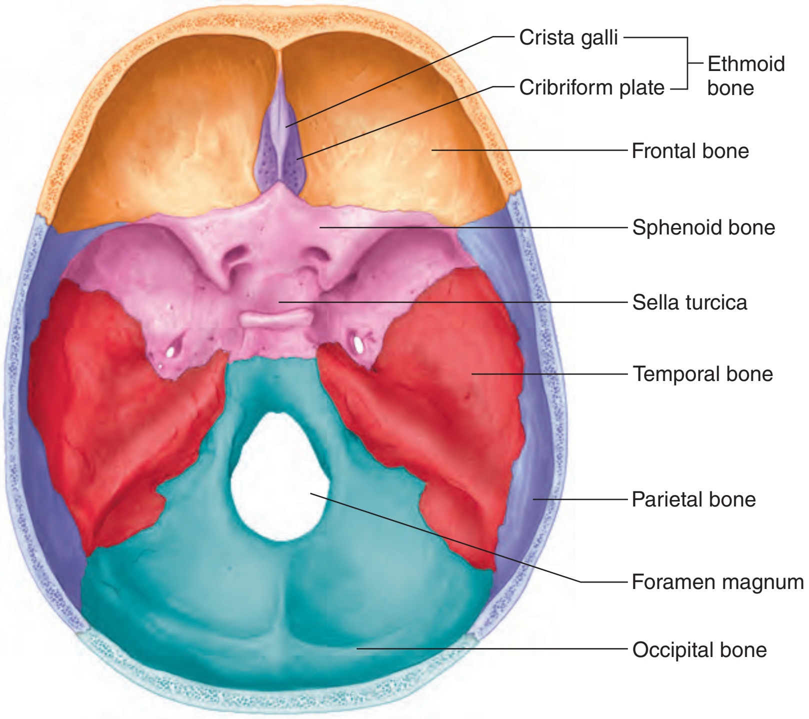

Crista galli
Cribriform plate
Ethmoid bone
Frontal bone
Sphenoid bone
Sella turcica
Temporal bone
Parietal bone
Foramen magnum
Occipital bone

**FIGURE 7.14** APIR Floor of the cranial cavity, viewed from above.

midline from the cribriform plates and forms most of the nasal septum (fig. 7.15).

Delicate scroll-shaped plates called the *superior nasal conchae* (kong′ke) and the *middle nasal conchae* project inward from the lateral portions of the ethmoid bone toward the perpendicular plate (see fig. 7.10). The lateral portions of the ethmoid bone contain many small spaces, the *ethmoidal air cells*, that together form the ethmoidal sinus (see fig. 7.11).

## Facial Skeleton

The **facial skeleton** consists of thirteen immovable bones and a movable lower jawbone. These bones form the basic shape of the face and provide attachments for muscles that move the jaw and control facial expressions.

The bones of the facial skeleton are:

1. **Maxillae.** The maxillae (mak-sil′e; singular, *maxilla,* mak-sil′ah) form the upper jaw (see figs. 7.12 and 7.13). Portions of these bones compose the anterior roof of the mouth (*hard palate*), the floors of the orbits, and the sides and floor of the nasal cavity. They also contain the sockets of the upper teeth. Inside the maxillae, lateral to the nasal cavity, are *maxillary sinuses,* the largest of the sinuses (see fig. 7.11).

   During development, portions of the maxillae called *palatine processes* grow together and fuse along the midline to form the anterior section of the hard palate. The inferior border of each maxillary bone projects downward, forming an *alveolar* (al-ve′o-lar) *process* (fig. 7.15). Together, these processes form a horseshoe-shaped *alveolar arch* (dental arch). Teeth occupy cavities (dental alveoli) in this arch. Dense connective tissue binds teeth to the bony sockets.

A *cleft palate* results from incomplete fusion of the palatine processes of the maxillae by the time of birth. An infant with a cleft palate may have trouble sucking a bottle due to the opening between the oral and nasal cavities. A temporary prosthetic device (artificial palate) worn in the mouth, or a special type of nipple placed on a bottle, can help the child eat and drink until surgery corrects the cleft. This surgery is most effective when performed between the ages of twelve and eighteen months.

2. **Palatine bones.** The L-shaped palatine (pal′ah-tīn) bones are located behind the maxillae (see figs. 7.13 and 7.15). The horizontal portions form the posterior section of the hard palate and the floor of the nasal cavity. The perpendicular portions help form the lateral walls of the nasal cavity.
3. **Zygomatic bones.** The zygomatic (zi″go-mat′ik) bones form the prominences of the cheeks below and to the sides of the eyes (see figs. 7.12 and 7.13). These bones also help form the lateral walls and the floors of the orbits. Each bone has a *temporal process,* which extends posteriorly to join the zygomatic process of a temporal bone. Together, these processes form a *zygomatic arch.*

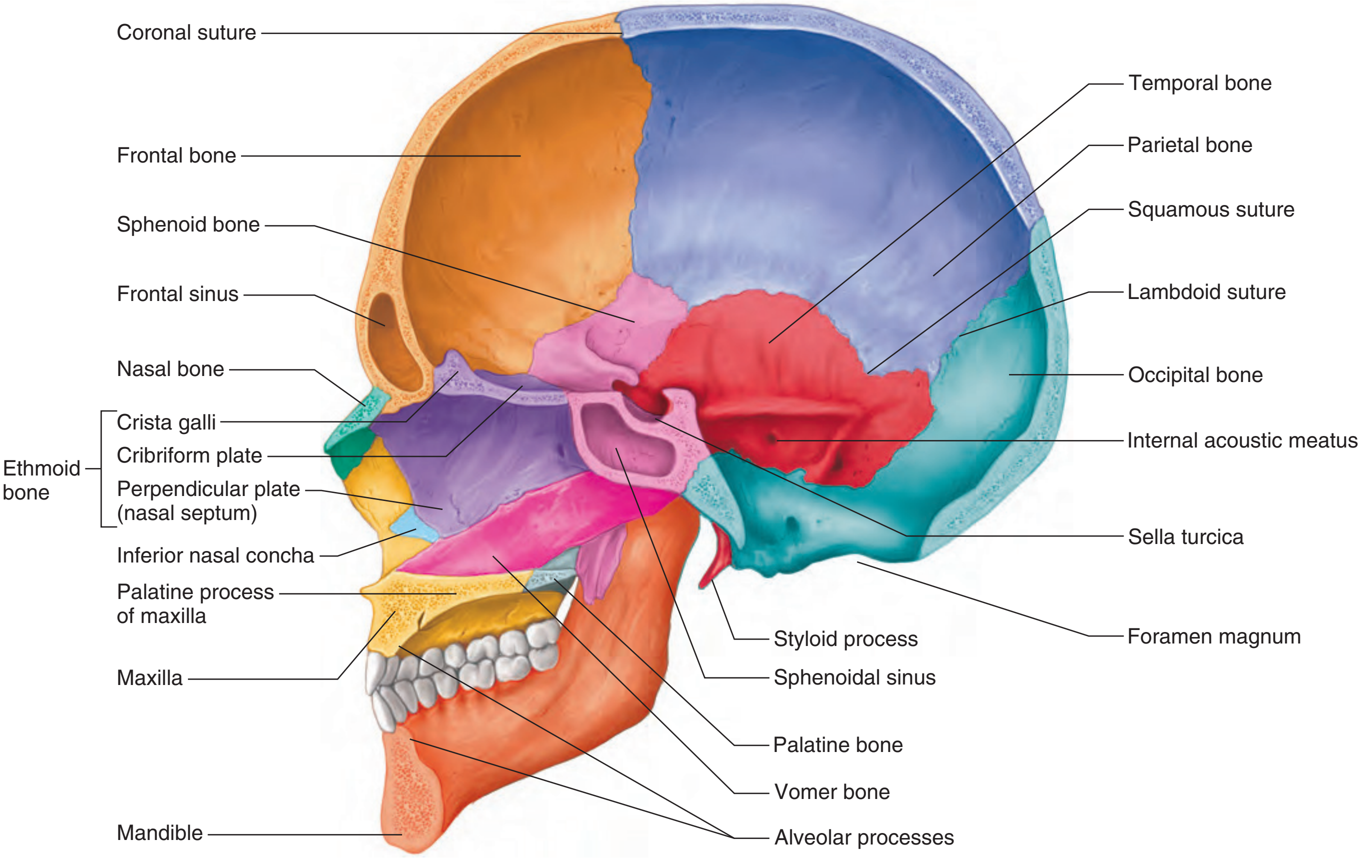

Coronal suture
Frontal bone
Sphenoid bone
Frontal sinus
Nasal bone
Ethmoid bone
Crista galli
Cribriform plate
Perpendicular plate (nasal septum)
Inferior nasal concha
Palatine process of maxilla
Maxilla
Mandible
Temporal bone
Parietal bone
Squamous suture
Lambdoid suture
Occipital bone
Internal acoustic meatus
Sella turcica
Foramen magnum
Styloid process
Sphenoidal sinus
Palatine bone
Vomer bone
Alveolar processes

**FIGURE 7.15** APR Sagittal section of the skull.

4. **Lacrimal bones.** A lacrimal (lak′rĭ-mal) bone is a thin, scalelike structure located in the medial wall of each orbit between the ethmoid bone and the maxilla (see figs. 7.10 and 7.12).
5. **Nasal bones.** The nasal (na′zal) bones are long, thin, and nearly rectangular (see figs. 7.10 and 7.12). They lie side by side and are fused at the midline, where they form the bridge of the nose.
6. **Vomer bone.** The thin, flat vomer (vo′mer) bone is located along the midline within the nasal cavity (see figs. 7.10 and 7.15). Posteriorly, it joins the perpendicular plate of the ethmoid bone, and together they form the nasal septum.
7. **Inferior nasal conchae.** The inferior nasal conchae are fragile, scroll-shaped bones attached to the lateral walls of the nasal cavity (see figs. 7.10 and 7.15). Like the superior and middle conchae of the ethmoid bone, the inferior conchae support mucous membranes in the nasal cavity.
8. **Mandible.** The mandible (man′dĭ-b′l) has a horizontal, horseshoe-shaped body with a vertical, flat portion projecting upward at each end (see figs. 7.10 and 7.12). This projection is divided into two processes—a posterior *mandibular condyle* and an anterior *coronoid process.* The mandibular condyles articulate with the mandibular fossae of the temporal bones (see fig. 7.13), whereas the coronoid processes provide attachments for muscles used in chewing. A curved bar of bone on the superior border of the mandible, the *alveolar arch,* contains the hollow sockets (dental alveoli) that bear the lower teeth.

## Infantile Skull

At birth the skull is incompletely developed, with fibrous membranes connecting the cranial bones. These membranous areas of incomplete intramembranous ossification are called **fontanels** (fon″tah-nelz′) or, more commonly, soft spots (fig. 7.16). They permit some movement between the bones, so that the developing skull is partially compressible and can slightly change shape. This enables an infant's skull to more easily pass through the birth canal. Eventually the fontanels close as the cranial bones grow together.

Other characteristics of an infantile skull include a relatively small face with a prominent forehead and large orbits. The jaw and nasal cavity are small, the sinuses are incompletely formed, and the frontal bone is in two parts. The skull bones are thin, but they are also somewhat flexible and thus are less easily fractured than adult skull bones.

### PRACTICE

15. Locate and name each of the bones of the cranium.
16. Locate and name each of the facial bones.
17. Explain how an adult skull differs from that of an infant.

## 7.7 | Vertebral Column

The **vertebral column** extends from the skull to the pelvis and forms the vertical axis of the skeleton. It is composed of many bony parts, called **vertebrae** (ver′tĕ-bre), that are separated by masses of fibrocartilage called *intervertebral discs* and are connected to one another by ligaments (fig. 7.17). The vertebral column supports the head and trunk of the body. It also protects the spinal cord, which passes through a *vertebral canal* formed by openings in the vertebrae.

### A Typical Vertebra

The vertebrae in different regions of the vertebral column have special characteristics, but they also have features in common. A typical vertebra has a drum-shaped *body,* which forms the thick, anterior portion of the bone (fig. 7.18). A longitudinal row of these vertebral bodies supports the weight of the head and trunk. The intervertebral discs, which separate adjacent vertebral bodies, cushion and soften the forces generated by such movements as walking and jumping.

Projecting posteriorly from each vertebral body are two short stalks called *pedicles* (ped′ĭ-k′lz). Two plates called *laminae* (lam′i-ne) arise from the pedicles and fuse in the back to become a *spinous process.* The pedicles, laminae, and spinous process together complete a bony *vertebral arch* around the *vertebral foramen,* through which the spinal cord passes.

If the laminae of the vertebrae do not unite during development, the vertebral arch remains incomplete, causing a condition called *spina bifida.* The contents of the vertebral canal protrude outward. Spina bifida is most common in the lumbosacral region. Folic acid supplements before and during pregnancy reduce the risk of spina bifida in the offspring.

Between the pedicles and laminae of a typical vertebra is a *transverse process,* which projects laterally and posteriorly. Ligaments and muscles are attached to the dorsal spinous process and the transverse processes. Projecting upward and downward from each vertebral arch are *superior* and *inferior articular processes.* These processes bear cartilage-covered facets by which each vertebra is joined to the one above and the one below it.

On the lower surfaces of the vertebral pedicles are notches that align with adjacent vertebrae to help form openings called *intervertebral foramina* (in″ter-ver′tĕ-bral fo-ram′ĭ-nah) (see fig. 7.17). These openings provide passageways for spinal nerves.

## Cervical Vertebrae

Seven **cervical vertebrae** compose the bony axis of the neck (see fig. 7.17). The transverse processes of these vertebrae are distinctive because they have *transverse foramina,* which are passageways for blood vessels to and from the brain (fig. 7.18*a*). Also, the spinous processes of the second through the sixth cervical vertebrae are uniquely forked (bifid). These processes provide attachments for muscles.

Two of the cervical vertebrae are of special interest: the atlas and the axis (fig. 7.19). The first vertebra, or **atlas** (at′las), supports the head. It has practically no body or spinous process and appears as a bony ring with two transverse processes. On its superior surface are two kidney-shaped *facets* that articulate with the occipital condyles.

The second cervical vertebra, or **axis** (ak′sis), bears a toothlike *dens* (odontoid process) on its body. This process projects upward and lies in the ring of the atlas. As the head is turned from side to side, the atlas pivots around the dens.

## Thoracic Vertebrae

The twelve **thoracic vertebrae** are larger than the cervical vertebrae (see fig. 7.17). Each vertebra has a long, pointed spinous process which slopes downward, and a facet on each side of its body which articulates with a rib (see fig. 7.18*b*).

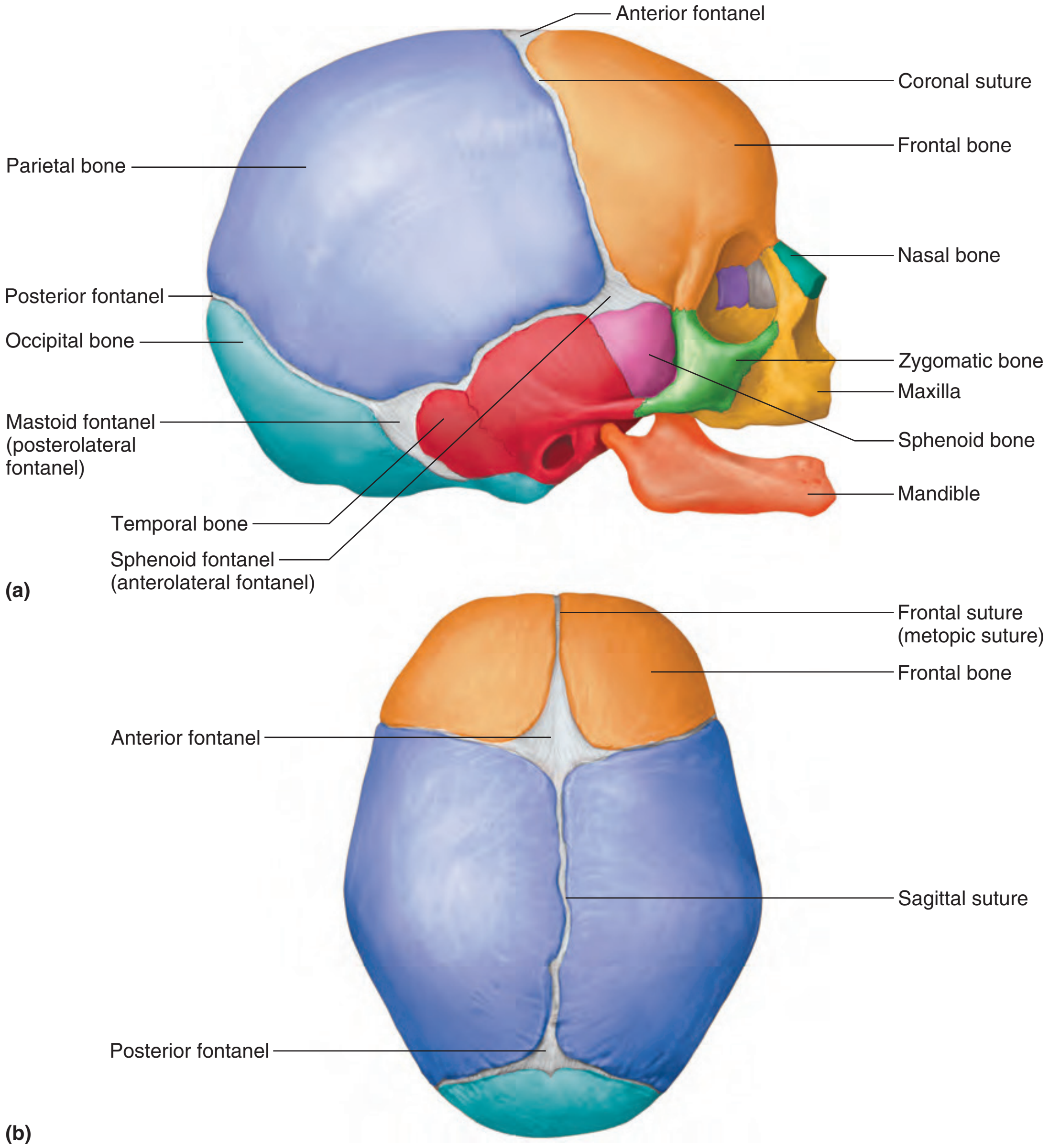

Anterior fontanel
Coronal suture
Frontal bone
Parietal bone
Nasal bone
Posterior fontanel
Occipital bone
Zygomatic bone
Maxilla
Mastoid fontanel (posterolateral fontanel)
Sphenoid bone
Mandible
Temporal bone
Sphenoid fontanel (anterolateral fontanel)
(a)
Frontal suture (metopic suture)
Frontal bone
Anterior fontanel
Sagittal suture
Posterior fontanel
(b)

**FIGURE 7.16** Fontanels. **(a)** Right lateral view and **(b)** superior view of the infantile skull.

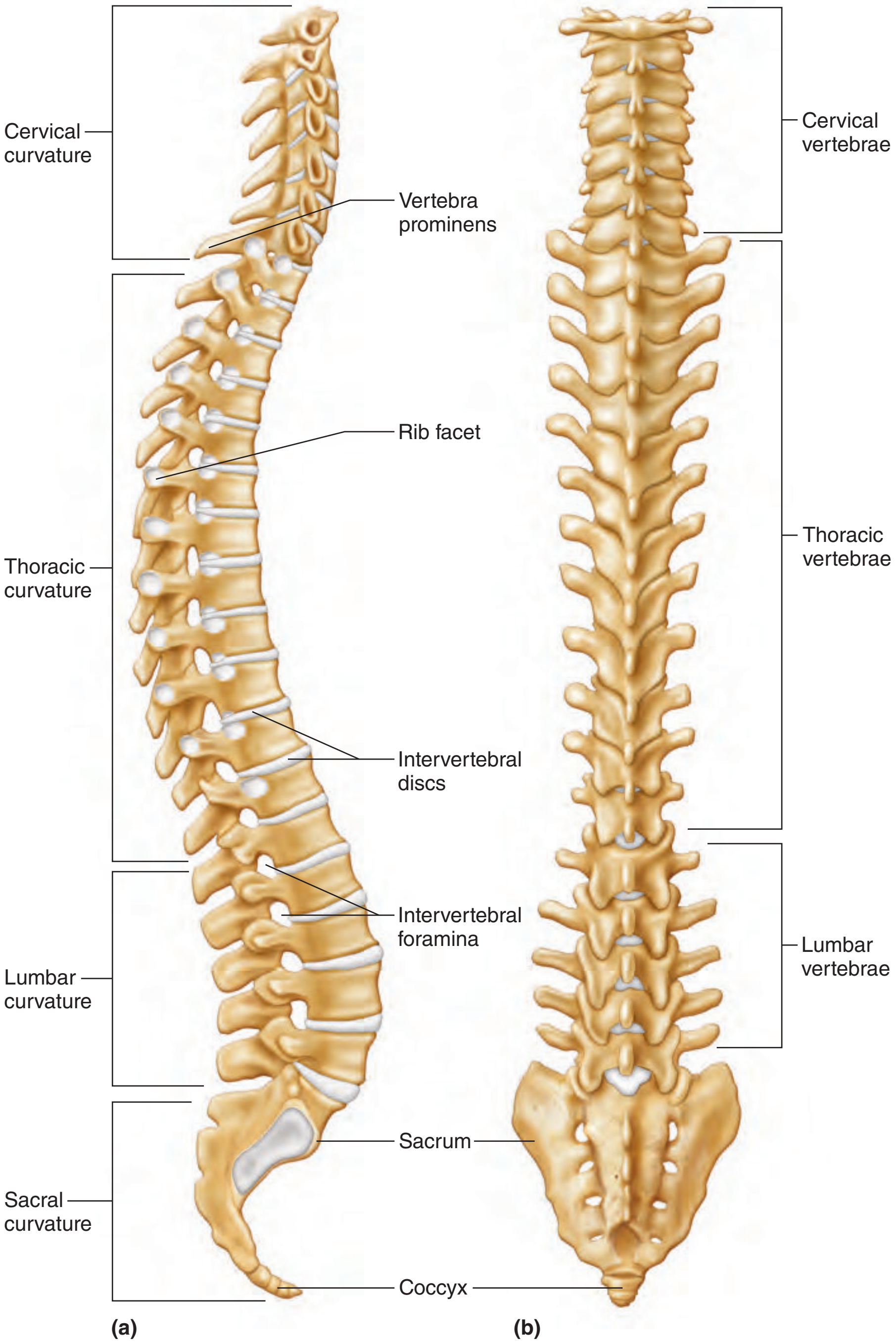

Cervical curvature
Vertebra prominens
Rib facet
Thoracic curvature
Intervertebral discs
Intervertebral foramina
Lumbar curvature
Sacrum
Sacral curvature
Coccyx
(a)
Cervical vertebrae
Thoracic vertebrae
Lumbar vertebrae
(b)

**FIGURE 7.17** APR The curved vertebral column consists of many vertebrae separated by intervertebral discs. **(a)** Right lateral view. **(b)** Posterior view.

Beginning with the third thoracic vertebra and moving inferiorly, the bodies of these bones increase in size. Thus, they are adapted to bear increasing loads of body weight.

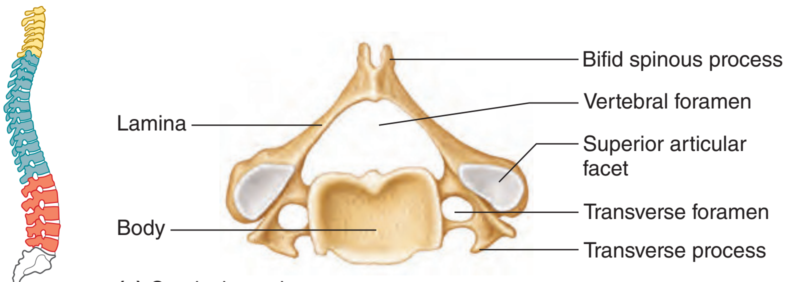
## Lumbar Vertebrae

Five **lumbar vertebrae** are in the small of the back (loin) (see fig. 7.17). These vertebrae are adapted with larger and stronger bodies to support more weight than the vertebrae above them (see fig. 7.18*c*).

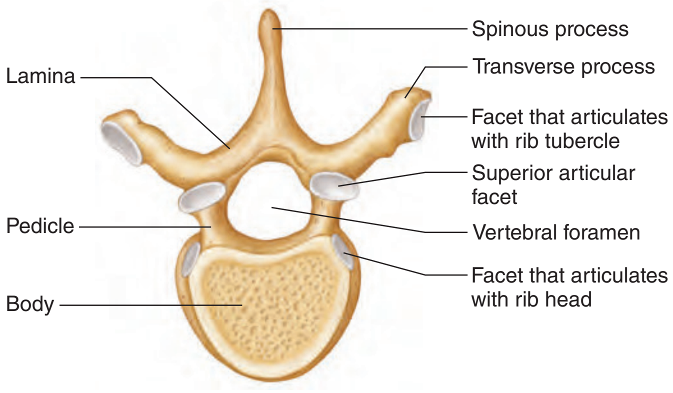
## Sacrum

The **sacrum** (sa′krum) is a triangular structure, composed of five fused vertebrae, that forms the base of the vertebral column (fig. 7.20). The spinous processes of these fused bones form a ridge of *tubercles.* To the sides of the tubercles are rows of openings, the *posterior sacral foramina,* through which nerves and blood vessels pass.

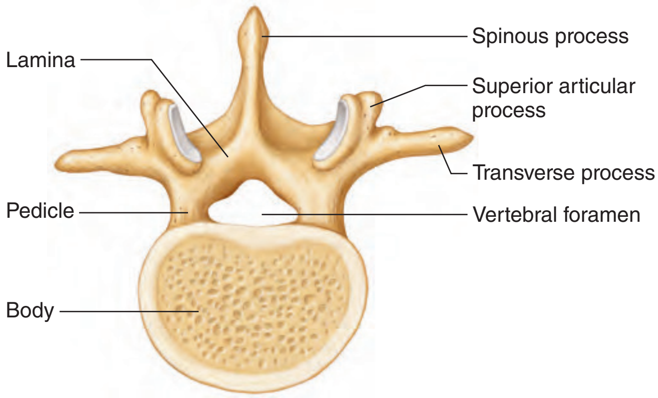
The vertebral foramina of the sacral vertebrae form the *sacral canal,* which continues through


Bifid spinous process
Vertebral foramen
Lamina
Superior articular facet
Transverse foramen
Body
Transverse process

**(a)** Cervical vertebra


Spinous process
Transverse process
Lamina
Facet that articulates with rib tubercle
Superior articular facet
Pedicle
Vertebral foramen
Facet that articulates with rib head
Body

**(b)** Thoracic vertebra


Spinous process
Lamina
Superior articular process
Transverse process
Pedicle
Vertebral foramen
Body

**(c)** Lumbar vertebra

**FIGURE 7.18** APR Superior view of **(a)** a cervical vertebra, **(b)** a thoracic vertebra, and **(c)** a lumbar vertebra.

the sacrum to an opening of variable size at the tip, called the *sacral hiatus* (sa′kral hi-a′tus). On the ventral surface of the sacrum, four pairs of *anterior sacral foramina* provide passageways for nerves and blood vessels.

## Coccyx

The **coccyx** (kok′siks), or tailbone, is the lowest part of the vertebral column and is usually composed of four fused vertebrae (fig. 7.20). Ligaments attach it to the margins of the sacral hiatus.

Changes in the intervertebral discs may cause various problems. Each disc is composed of a tough outer layer of fibrocartilage and an elastic central mass. With age, these discs degenerate—the central masses lose firmness, and the outer layers thin and weaken, developing cracks. Extra pressure, as when a person falls or lifts a heavy object, can break the outer layer of a disc, squeezing out the central mass. Such a rupture may press on the spinal cord or on a spinal nerve that branches from it. This condition—a ruptured or herniated disc—may cause back pain and numbness or loss of muscular function in the parts innervated by the affected spinal nerve.

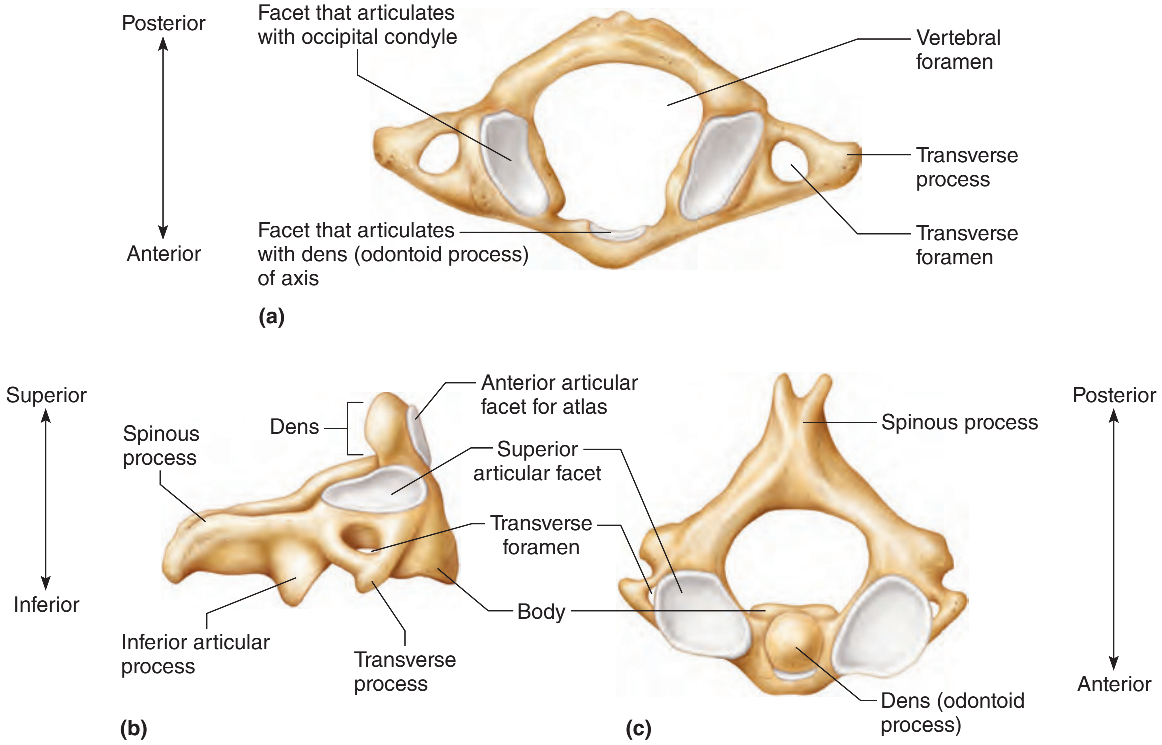

Posterior
Anterior
Facet that articulates with occipital condyle
Vertebral foramen
Transverse process
Transverse foramen
Facet that articulates with dens (odontoid process) of axis
(a)
Superior
Inferior
Spinous process
Dens
Anterior articular facet for atlas
Superior articular facet
Transverse foramen
Body
Inferior articular process
Transverse process
(b)
Spinous process
Posterior
Anterior
Dens (odontoid process)
(c)

**FIGURE 7.19** APIR Atlas and axis. **(a)** Superior view of the atlas. **(b)** Right lateral view and **(c)** superior view of the axis.

**PRACTICE**

18. Describe the structure of the vertebral column.
19. Describe a typical vertebra.
20. Explain how the structures of cervical, thoracic, and lumbar vertebrae differ.

## 7.8 | Thoracic Cage

The **thoracic cage** includes the ribs, the thoracic vertebrae, the sternum, and the costal cartilages that attach the ribs to the sternum (fig. 7.21). These bones support the pectoral girdle and upper limbs, protect the viscera in the thoracic and upper abdominal cavities, and play a role in breathing.

### Ribs

The usual number of **ribs** is twenty-four—one pair attached to each of the twelve thoracic vertebrae. The first seven rib pairs, *true ribs* (vertebrosternal ribs), join the sternum directly by their costal cartilages. The remaining five pairs are called *false ribs,* because their cartilages do not reach the sternum directly. Instead, the cartilages of the upper three false ribs (vertebrochondral ribs) join the cartilages of the seventh rib. The last two (or sometimes three) rib pairs are called *floating ribs* (vertebral ribs) because they have no cartilaginous attachments to the sternum.

A typical rib has a long, slender shaft, which curves around the chest and slopes downward. On the posterior end is an enlarged *head* by which the rib articulates with a *facet* on the body of its own vertebra and with the body of the next higher vertebra. A *tubercle,* close to the head of the rib, articulates with the transverse process of the vertebra.

### Sternum

The **sternum,** or breastbone, is located along the midline in the anterior portion of the thoracic cage (fig. 7.21). This flat, elongated bone develops in three parts—an upper *manubrium* (mah-nu′bre-um), a middle *body,* and a lower *xiphoid* (zīf′oid) *process* that projects downward. The manubrium articulates with the clavicles by facets on its superior border.

**PRACTICE**

21. Which bones compose the thoracic cage?
22. What are the differences among true, false, and floating ribs?
23. Name the three parts of the sternum.

## 7.9 | Pectoral Girdle

The **pectoral girdle,** or shoulder girdle, is composed of four parts—two clavicles and two scapulae (fig. 7.22). Although the word *girdle* suggests a ring-shaped struc-

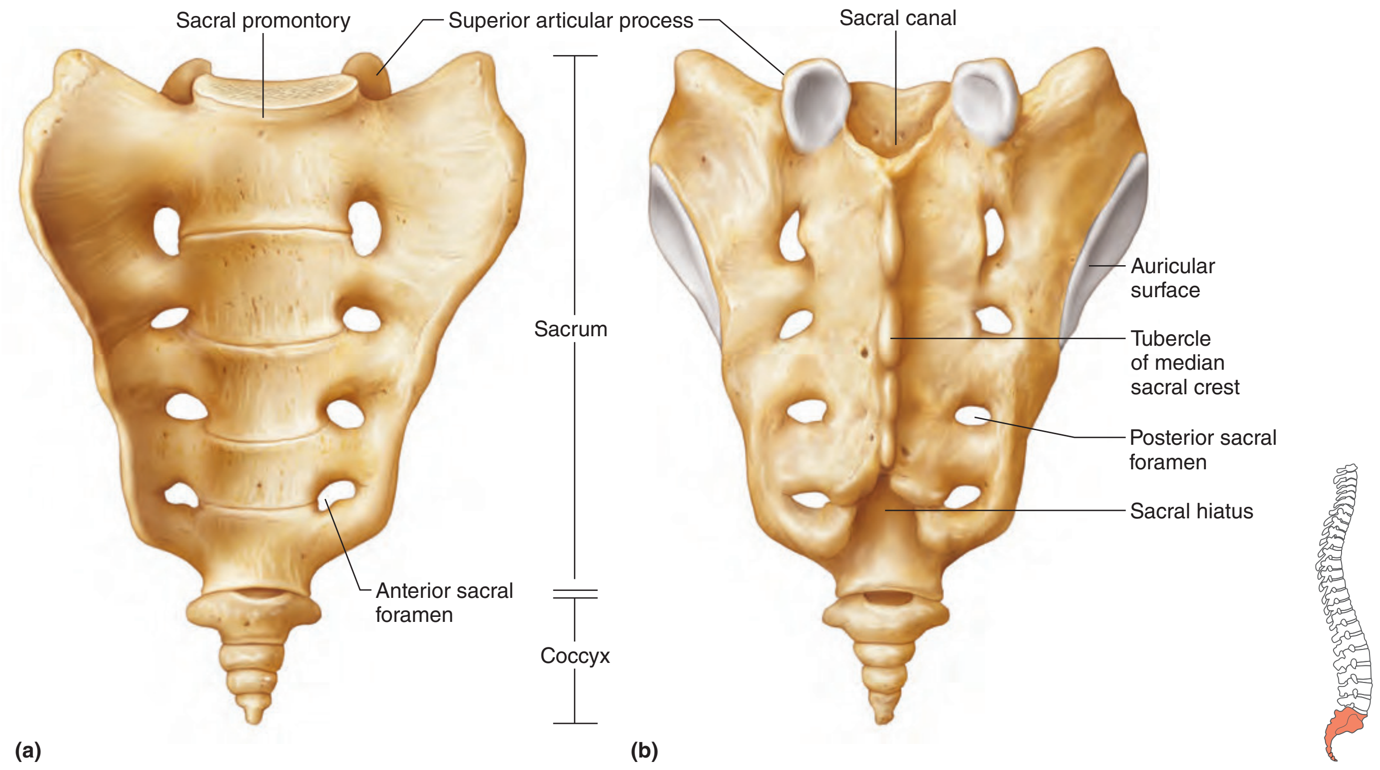

Sacral promontory
Superior articular process
Sacral canal
Sacrum
Auricular surface
Tubercle of median sacral crest
Posterior sacral foramen
Sacral hiatus
Anterior sacral foramen
Coccyx
(a)
(b)

**FIGURE 7.20** Sacrum and coccyx. **(a)** Anterior view and **(b)** posterior view.

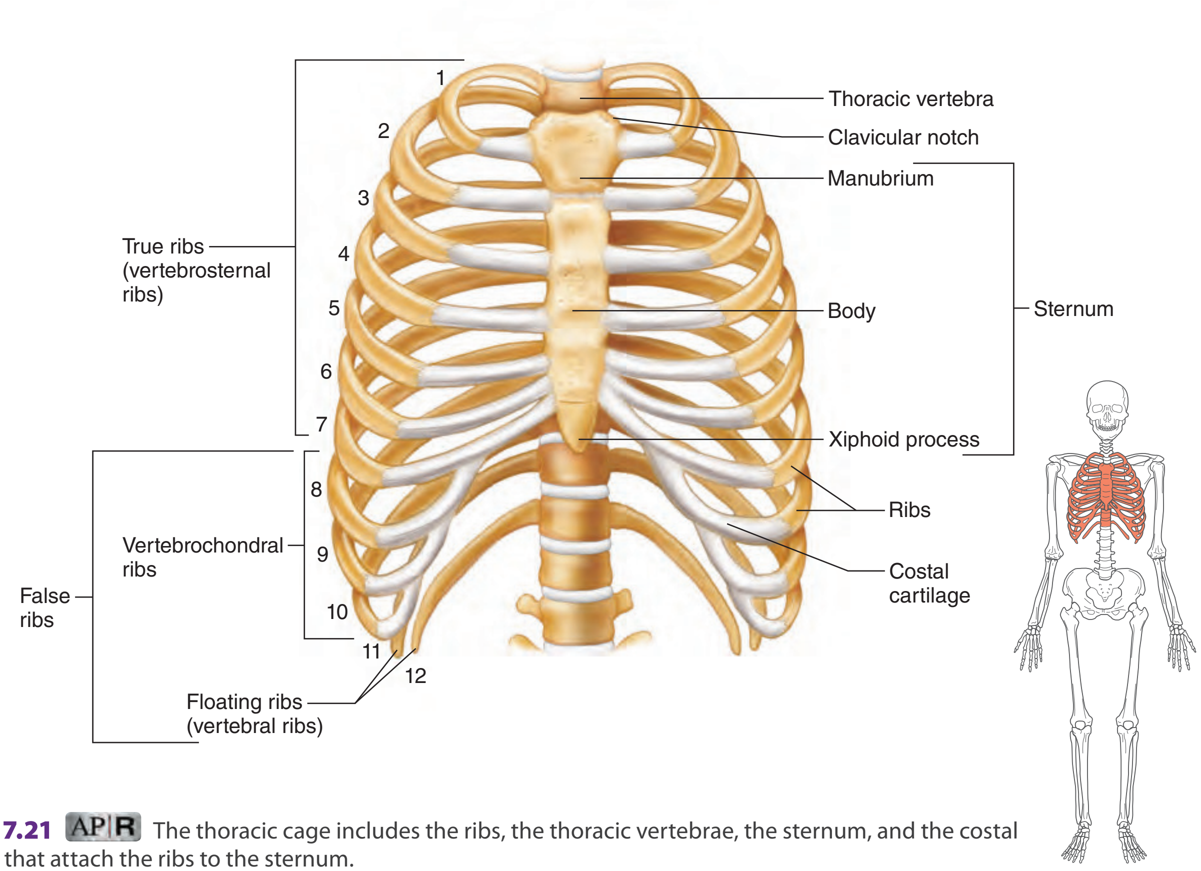

1
2
3
4
5
6
7
8
9
10
11
12
True ribs (vertebrosternal ribs)
Vertebrochondral ribs
False ribs
Floating ribs (vertebral ribs)
Thoracic vertebra
Clavicular notch
Manubrium
Body
Xiphoid process
Sternum
Ribs
Costal cartilage

**FIGURE 7.21** The thoracic cage includes the ribs, the thoracic vertebrae, the sternum, and the costal cartilages that attach the ribs to the sternum.

ture, the pectoral girdle is an incomplete ring. It is open in the back between the scapulae, and the sternum separates its bones in front. The pectoral girdle supports the upper limbs and is an attachment for several muscles that move them.

### Clavicles

The **clavicles,** or collarbones, are slender, rodlike bones with elongated S shapes (fig. 7.22). Located at the base of the neck, they run horizontally between the manubrium and the scapulae.

The clavicles brace the freely movable scapulae, helping to hold the shoulders in place. They also provide attachments for muscles of the upper limbs, chest, and back.

### Scapulae

The **scapulae** (skap′u-le), or shoulder blades, are broad, somewhat triangular bones located on either side of the upper back (figs. 7.22 and 7.23). A *spine* divides the posterior surface of each scapula into unequal portions. This spine leads to an *acromion* (ah-kro′me-on) *process* that forms the tip of the shoulder. The acromion process articulates with the clavicle and provides attachments for muscles of the upper limb and chest. A *coracoid* (kor′ah-koid) *process* curves anteriorly and inferiorly to the clavicle. The coracoid process also provides attachments for upper limb and chest muscles. On the lateral surface of the scapula and between these processes is a depression called the *glenoid cavity* (glenoid fossa of the scapula) that articulates with the head of the arm bone (humerus).

**PRACTICE**

24. Which bones form the pectoral girdle?
25. What is the function of the pectoral girdle?

## 7.10 | Upper Limb

The bones of the upper limb form the framework of the arm, forearm, and hand. They also provide attachments for muscles and interact with muscles to move limb parts. These bones include a humerus, a radius, an ulna, carpals, metacarpals, and phalanges (see fig. 7.9).

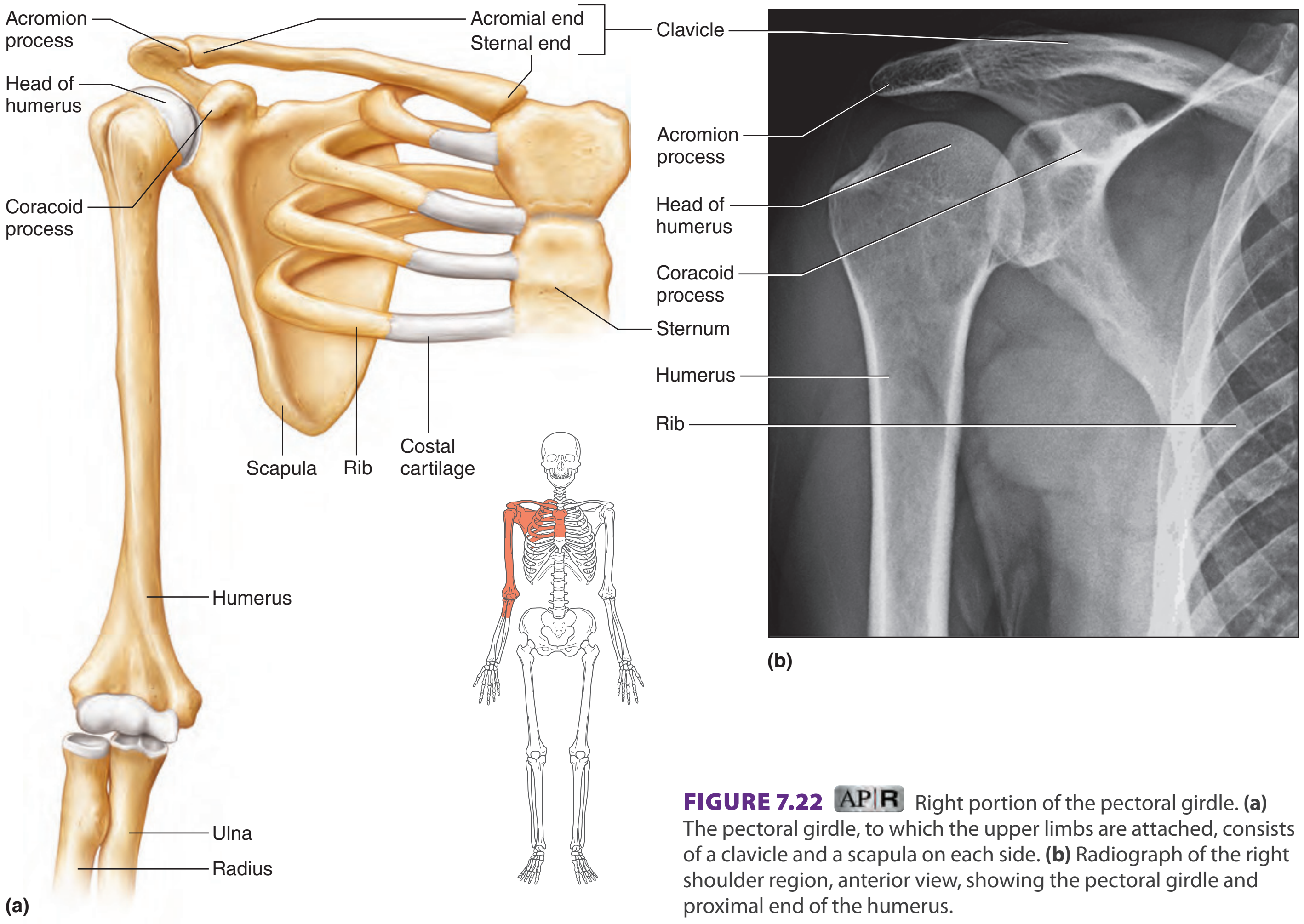


**FIGURE 7.22** APR Right portion of the pectoral girdle. **(a)** The pectoral girdle, to which the upper limbs are attached, consists of a clavicle and a scapula on each side. **(b)** Radiograph of the right shoulder region, anterior view, showing the pectoral girdle and proximal end of the humerus.

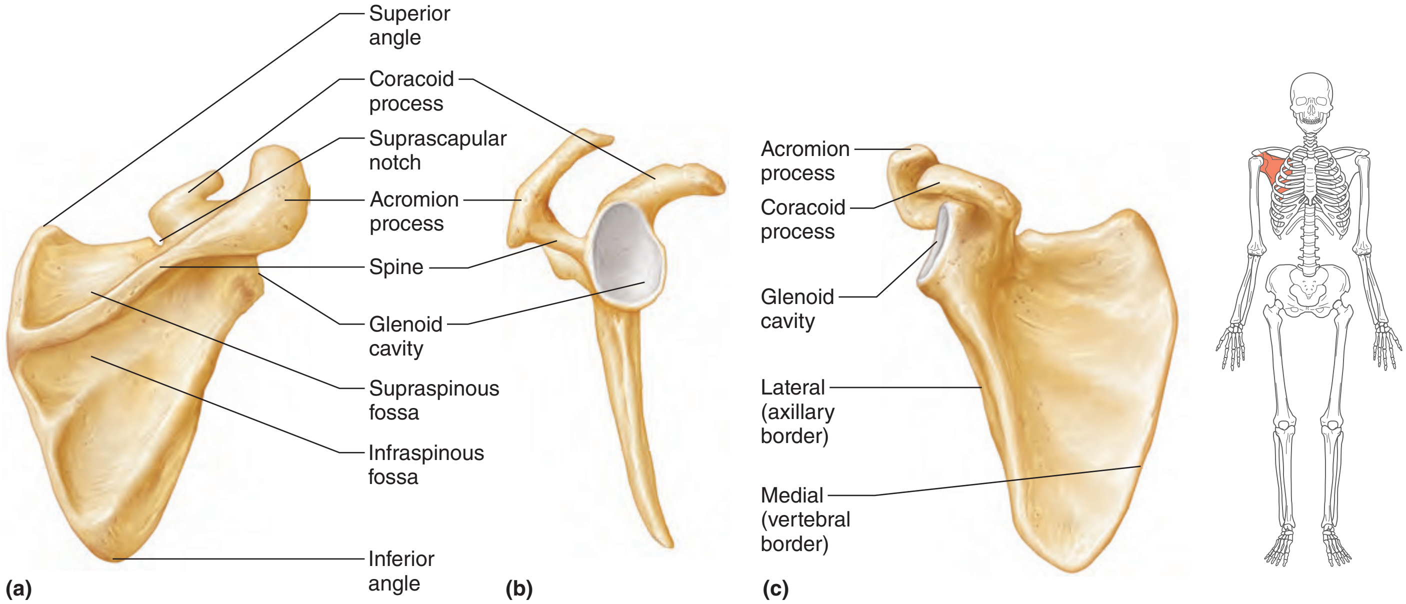


**FIGURE 7.23** Right scapula. **(a)** Posterior surface. **(b)** Lateral view showing the glenoid cavity that articulates with the head of the humerus. **(c)** Anterior surface.

## Humerus

The **humerus** is a long bone that extends from the scapula to the elbow (fig. 7.24). At its upper end is a smooth, rounded *head* that fits into the glenoid cavity of the scapula. Just below the head are two processes—a *greater tubercle* on the lateral side and a *lesser tubercle* on the anterior side. These tubercles provide attachments for muscles that move the upper limb at the shoulder. Between them is a narrow furrow, the *intertubercular sulcus* (intertubercular groove).

The narrow depression along the lower margin of the humerus head that separates it from the tubercles is called the *anatomical neck.* Just below the head and the tubercles is a tapering region called the *surgical neck,* so named because fractures commonly occur there. Near the middle of the bony shaft on the lateral side is a rough, V-shaped area called the *deltoid tuberosity.* It provides an attachment for the muscle (deltoid) that raises the upper limb horizontally to the side.

At the lower end of the humerus are two smooth *condyles* (a lateral *capitulum* and a medial *trochlea*) that articulate with the radius on the lateral side and the ulna on the medial side. Above the condyles on either side are *epicondyles,* which provide attachments for muscles and ligaments of the elbow. Between the epicondyles anteriorly is a depression, the *coronoid* (kor′o-noid) *fossa,* that receives a process of the ulna (coronoid process) when the elbow bends. Another depression on the posterior surface, the *olecranon* (o″lek′ra-non) *fossa,* receives a different ulnar process, the olecranon process, when the elbow straightens.

## Radius

The **radius,** located on the thumb side of the forearm, extends from the elbow to the wrist and crosses over the ulna when the hand is turned so that the palm faces backward (fig. 7.25). A thick, disclike *head* at the upper end of the radius articulates with the humerus and a notch of the ulna (radial notch). This arrangement allows the radius to rotate.

On the radial shaft just below the head is a process called the *radial tuberosity.* It is an attachment for a muscle (biceps brachii) that bends the upper limb at the elbow. At the distal end of the radius, a lateral *styloid* (sti′loid) *process* provides attachments for ligaments of the wrist.

## Ulna

The **ulna** is longer than the radius and overlaps the end of the humerus posteriorly (fig. 7.25). At its proximal end, the ulna has a wrenchlike opening, the *trochlear* (trok′le-ar) *notch,* that articulates with the humerus. Two processes above and below this notch, the *olecranon process* and the *coronoid process,* provide attachments for muscles.

At the distal end of the ulna, its knoblike *head* articulates laterally with a notch of the radius (ulnar notch) and with a disc of fibrocartilage inferiorly. This disc, in turn, joins a wrist bone (triquetrum). A medial *styloid process* at the distal end of the ulna provides attachments for wrist ligaments.

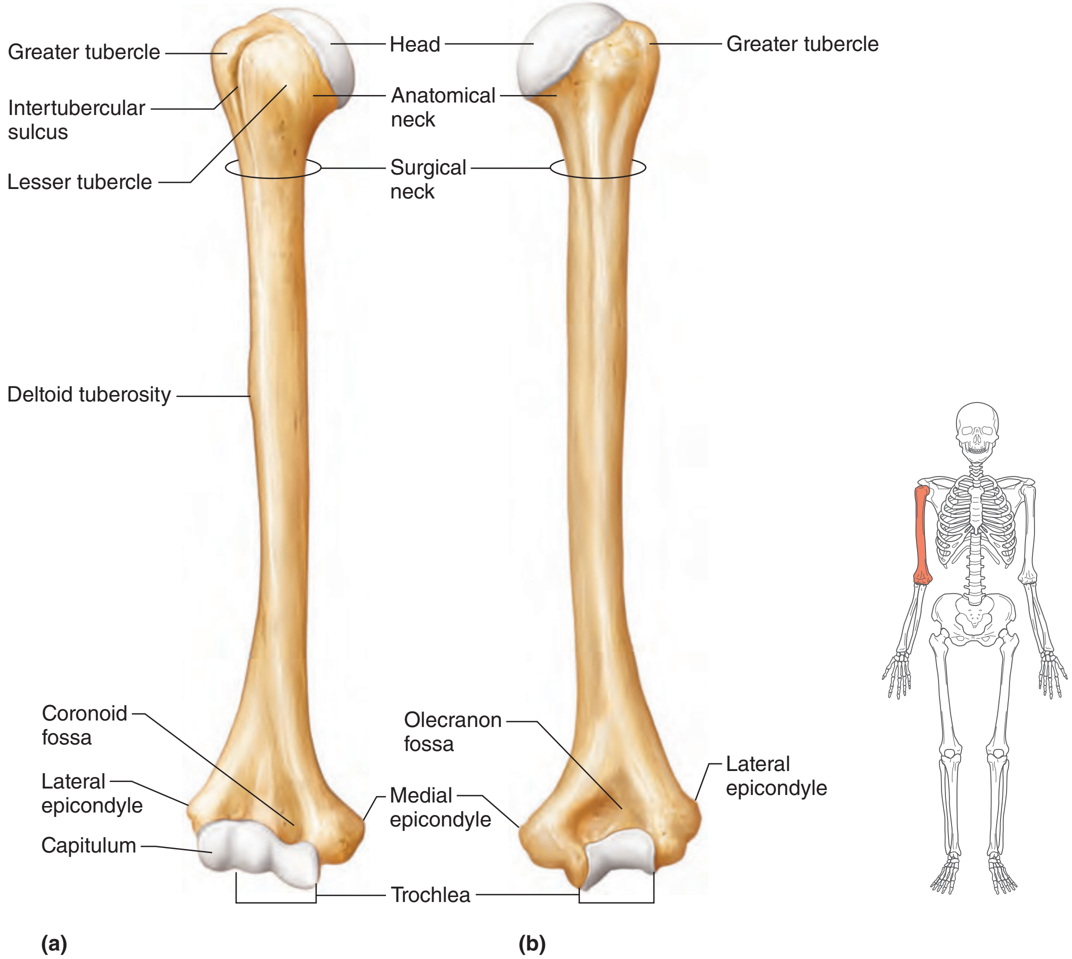

Greater tubercle
Intertubercular sulcus
Lesser tubercle
Head
Anatomical neck
Surgical neck
Greater tubercle
Deltoid tuberosity
Coronoid fossa
Lateral epicondyle
Capitulum
Olecranon fossa
Medial epicondyle
Trochlea
Lateral epicondyle
(a)
(b)

**FIGURE 7.24** APR Right humerus. **(a)** Anterior surface. **(b)** Posterior surface.

## Hand

The hand is made up of the wrist, palm, and fingers. The skeleton of the wrist consists of eight small **carpal bones** firmly bound in two rows of four bones each. The resulting compact mass is called a *carpus* (kar′pus). The carpus articulates with the radius and with the fibrocartilaginous disc on the ulnar side. Its distal surface articulates with the metacarpal bones. Figure 7.26 names the individual bones of the carpus.

Five **metacarpal bones,** one in line with each finger, form the framework of the palm or *metacarpus* (met″ah-kar′pus) of the hand. These bones are cylindrical, with rounded distal ends that form the knuckles of a clenched fist. They are numbered 1–5, beginning with the metacarpal of the thumb (fig. 7.26). The metacarpals articulate proximally with the carpals and distally with the phalanges.

The **phalanges** are the finger bones. Each finger has three phalanges—a proximal, a middle, and a distal phalanx—except the thumb, which has two (it lacks a middle phalanx).

**PRACTICE**

26. Locate and name each of the bones of the upper limb.
27. Explain how the bones of the upper limb articulate.

## 7.11 | Pelvic Girdle

The **pelvic girdle** consists of two hip bones (coxal bones, pelvic bones, or innominate bones) that articulate with each other anteriorly and with the sacrum posteriorly. The sacrum, coccyx, and pelvic girdle together form the bowl-shaped **pelvis** (fig. 7.27). The pelvic girdle supports the trunk of the body, provides attachments for the lower limbs, and protects the urinary bladder, the distal end of the large intestine, and the internal reproductive organs.

Each hip bone develops from three parts—an ilium, an ischium, and a pubis (fig. 7.28). These parts fuse in the region of a cup-shaped cavity called the *acetabulum* (as″ĕ-tab′u-lum). This depression, on the lateral sur-

**FIGURE 7.25** Right radius and ulna. **(a)** The head of the radius articulates with the radial notch of the ulna, and the head of the ulna articulates with the ulnar notch of the radius. **(b)** Lateral view of the proximal end of the ulna.

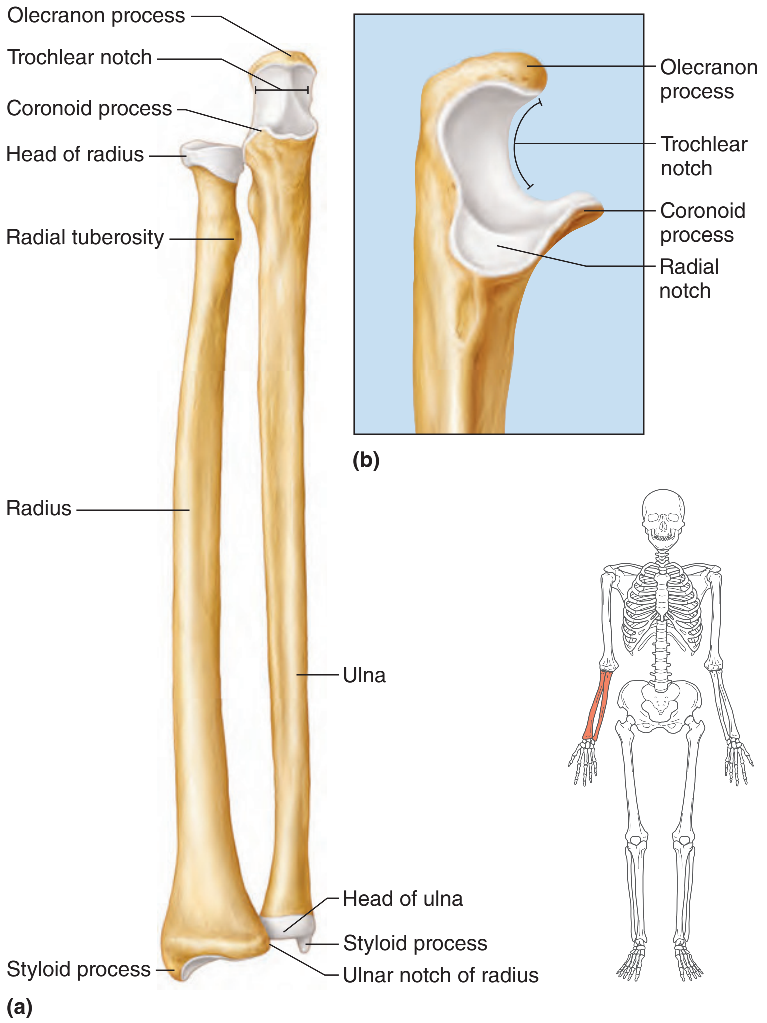
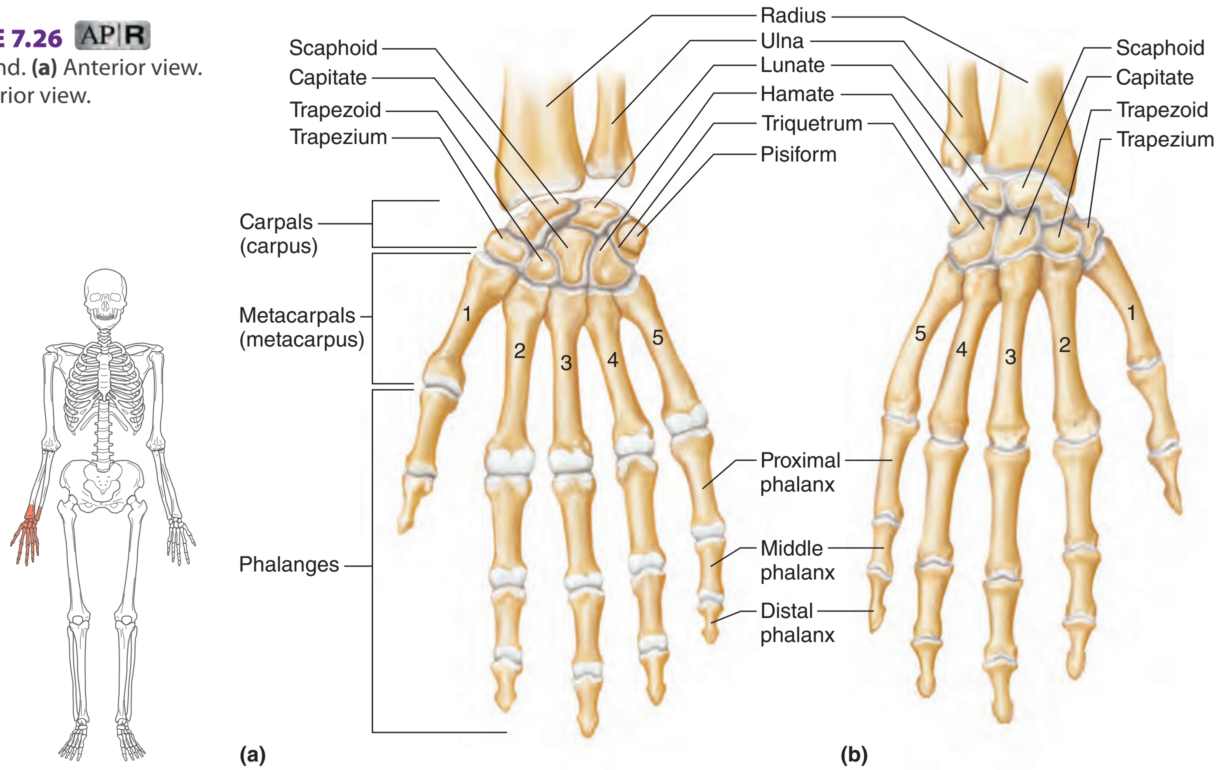

Olecranon process
Trochlear notch
Coronoid process
Head of radius
Radial tuberosity
Radius
Ulna
Head of ulna
Styloid process
Ulnar notch of radius
Styloid process
(a)
Olecranon process
Trochlear notch
Coronoid process
Radial notch
(b)

**FIGURE 7.26** Right hand. **(a)** Anterior view. **(b)** Posterior view.


Scaphoid
Capitate
Trapezoid
Trapezium
Carpals (carpus)
Metacarpals (metacarpus)
Phalanges
Radius
Ulna
Lunate
Hamate
Triquetrum
Pisiform
1
2
3
4
5
Proximal phalanx
Middle phalanx
Distal phalanx
Scaphoid
Capitate
Trapezoid
Trapezium
5
4
3
2
1
(a)
(b)

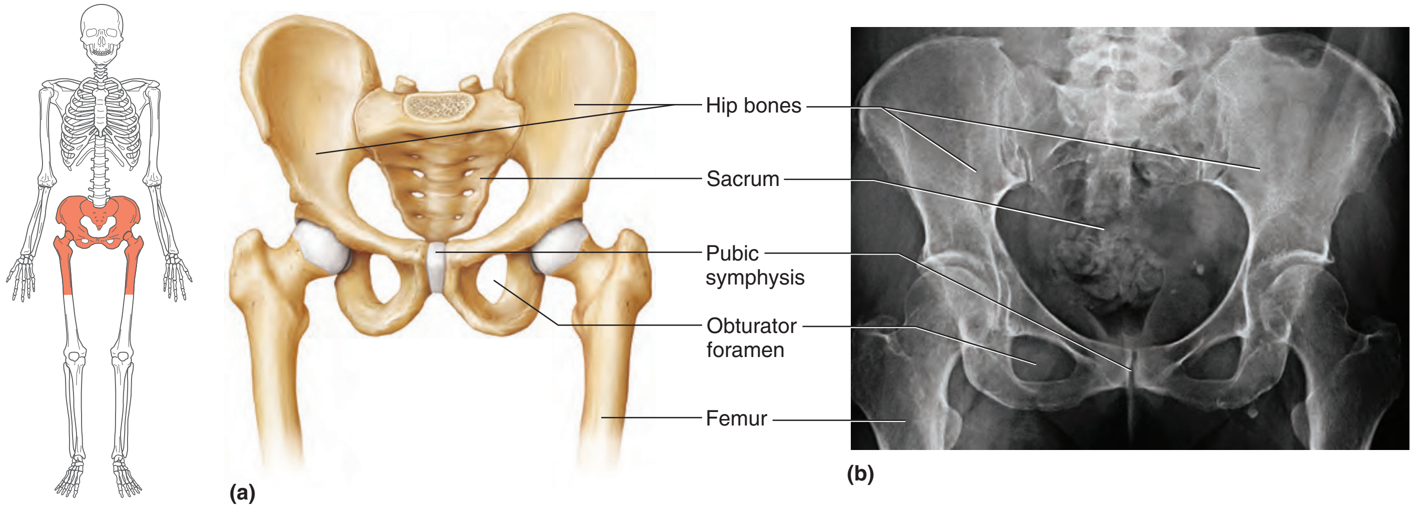

Hip bones
Sacrum
Pubic symphysis
Obturator foramen
Femur
(a)
(b)

**FIGURE 7.27** APR Pelvic girdle. **(a)** The pelvic girdle is formed by two hip bones. The pelvis includes the pelvic girdle as well as the sacrum and the coccyx. **(b)** Radiograph of the pelvic girdle showing the sacrum, coccyx, and proximal ends of the femurs.

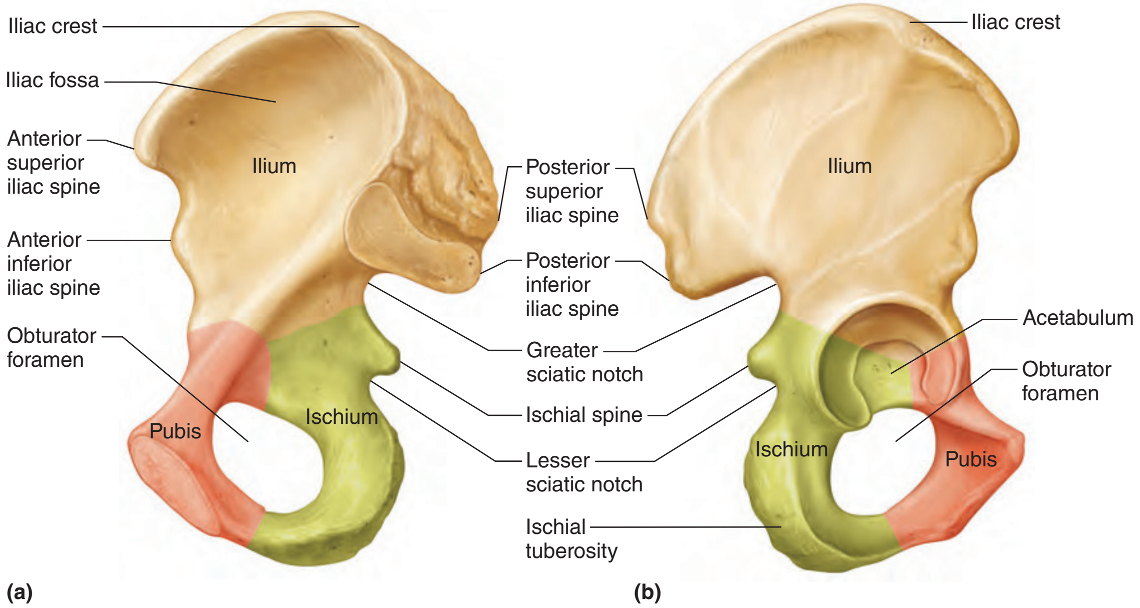

Iliac crest
Iliac fossa
Anterior superior iliac spine
Anterior inferior iliac spine
Obturator foramen
Ilium
Pubis
Ischium
Posterior superior iliac spine
Posterior inferior iliac spine
Greater sciatic notch
Ischial spine
Lesser sciatic notch
Ischial tuberosity
Iliac crest
Ilium
Acetabulum
Obturator foramen
Ischium
Pubis
(a)
(b)

**FIGURE 7.28** APR Right hip bone. **(a)** Medial surface. **(b)** Lateral view.

face of the hip bone, receives the rounded head of the femur (thigh bone).

The **ilium** (il′e-um), which is the largest and uppermost portion of the hip bone, flares outward, forming the prominence of the hip. The margin of this prominence is called the *iliac crest.*

Posteriorly, the ilium joins the sacrum at the *sacroiliac* (sa″kro-il′e-ak) *joint.* Anteriorly, a projection of the ilium, the *anterior superior iliac spine,* can be felt lateral to the groin and provides attachments for ligaments and muscles.

The **ischium** (is′ke-um), which forms the lowest portion of the hip bone, is L-shaped, with its angle, the *ischial tuberosity,* pointing posteriorly and downward. This tuberosity has a rough surface that provides attachments for ligaments and lower limb muscles. It also supports the weight of the body during sitting. Above the ischial tuberosity, near the junction of the ilium and ischium, is a sharp projection called the *ischial spine.* The distance between the ischial spines is the shortest diameter of the pelvic outlet.

The **pubis** (pu′bis) constitutes the anterior portion of the hip bone. The two pubic bones come together at the midline, to form a joint called the *pubic symphysis* (pu′bik sim′fi-sis). The angle these bones form below the symphysis is the *pubic arch* (fig. 7.29).

A portion of each pubis passes posteriorly and downward to join an ischium. Between the bodies of these bones on either side is a large opening, the *obturator foramen,* which is the largest foramen in the skeleton (see figs. 7.27 and 7.28).

If a line were drawn along each side of the pelvis from the sacral promontory downward and anteriorly to the upper margin of the pubic symphysis, it would mark the *pelvic brim* (linea terminalis) (fig. 7.29). Table 7.3 summarizes some differences in the female and male pelves and other skeletal structures.

## PRACTICE

28. Locate and name each bone that forms the pelvis.
29. Name the bones that fuse to form a hip bone.

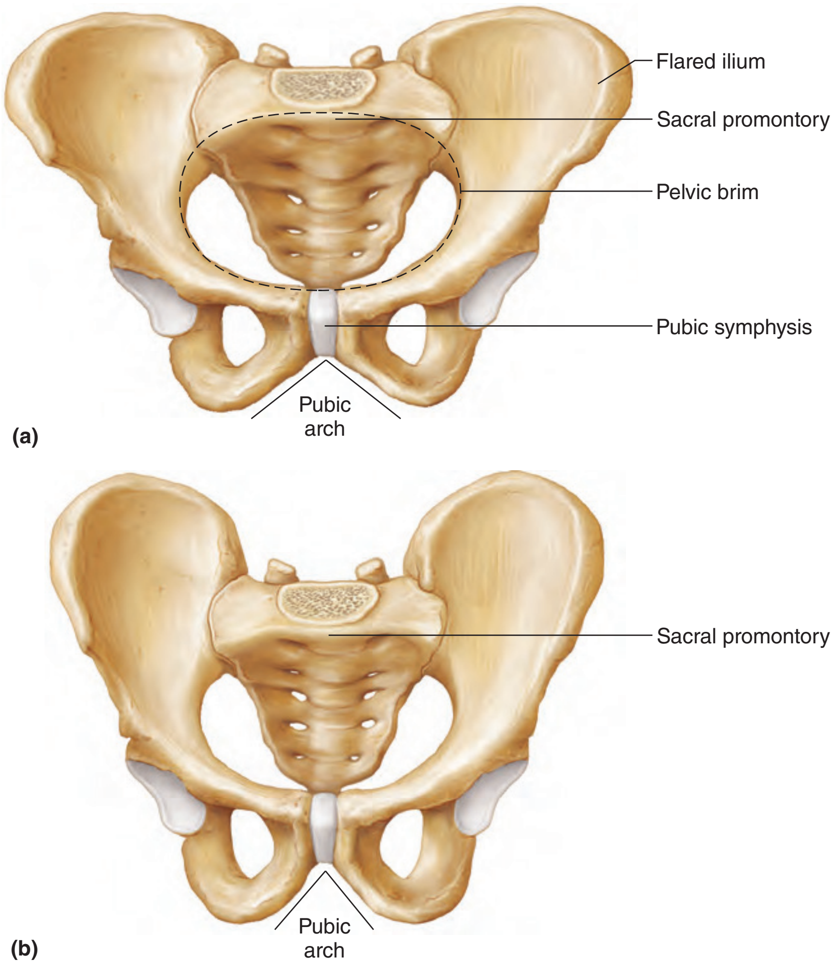


**FIGURE 7.29** The female pelvis is usually wider in all diameters and roomier than that of the male. **(a)** Female pelvis. **(b)** Male pelvis.

Q *Looking at the figure, what are some of the specific differences that can be observed between the male pelvis and female pelvis?*
**Answer can be found in Appendix F on page 582.**

## TABLE 7.3 Differences Between the Female and Male Skeletons

| Part | Differences |
|---|---|
| Skull | Female skull is smaller and lighter, with less evidence of muscular attachments. The female chin is more pointed, palate is narrower, and mastoid process is less prominent than those of a male. |
| Pelvic girdle | Female hip bones are lighter, thinner, and have less evidence of muscular attachments. The female obturator foramina are triangular, whereas the male's are oval. The female acetabula are smaller and the pubic arch is wider than those of a male. |
| Pelvic cavity | Female pelvic cavity is wider in all diameters and is shorter, roomier, and less funnel-shaped. The distances between the female ischial spines and ischial tuberosities are greater than in a male. |
| Sacrum | Female sacrum is wider, and the sacral curvature is bent more sharply posteriorly than in a male. |
| Coccyx | Female coccyx is more movable than that of a male. |

## 7.12 | Lower Limb

Bones of the lower limb form the frameworks of the thigh, leg, and foot. They include a femur, a tibia, a fibula, tarsals, metatarsals, and phalanges (see fig. 7.9).

### Femur

The **femur,** or thigh bone, is the longest bone in the body and extends from the hip to the knee (fig. 7.30). A large, rounded *head* at its proximal end projects medially into the acetabulum of the hip bone. On the head, a pit called the *fovea capitis* marks the attachment of a ligament (ligamentum capitis). Just below the head are a constriction, or *neck,* and two large processes—a superior, lateral *greater trochanter* and an inferior, medial *lesser trochanter.* These processes provide attachments for muscles of the lower limbs and buttocks.

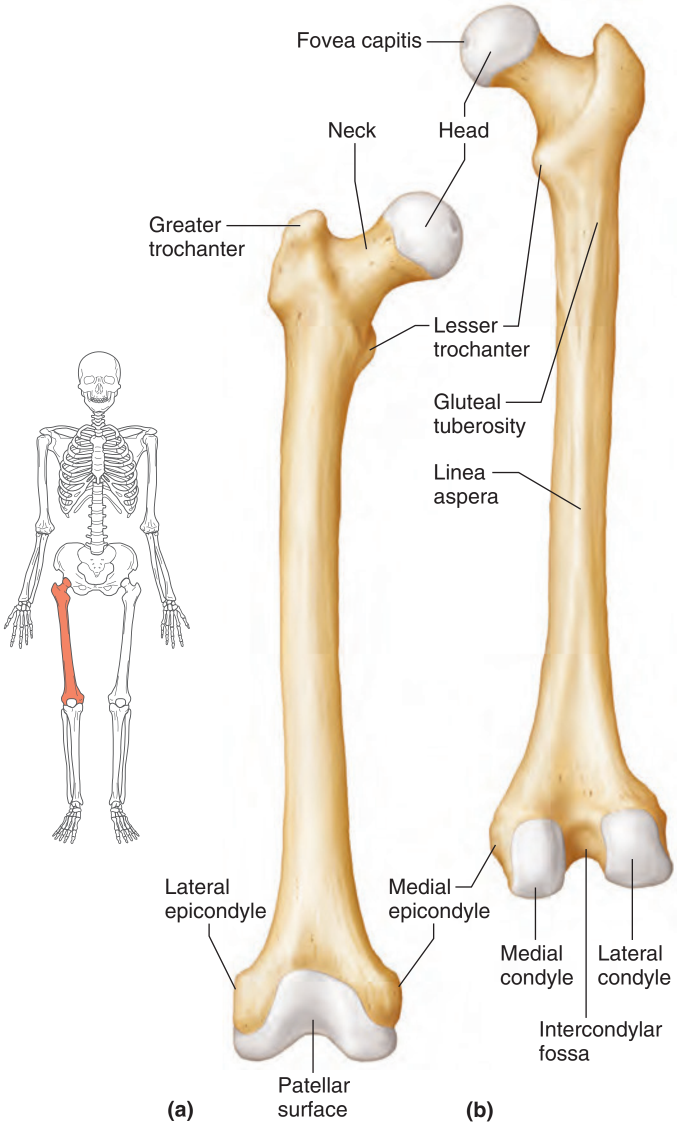


**FIGURE 7.30** APR Right femur. **(a)** Anterior surface. **(b)** Posterior surface.

**FACTS OF LIFE** The strongest bone in the body, the femur, has greater pressure tolerance and bearing strength than a rod of equivalent weight made of cast steel.

At the distal end of the femur, two rounded processes, the *lateral* and *medial condyles,* articulate with the tibia of the leg. A **patella,** or kneecap, also articulates with the femur on its distal anterior surface (see fig. 7.9). The patella is located in a tendon that passes anteriorly over the knee.

*Hip fracture* is one of the more serious causes of hospitalization among elderly persons. The site of hip fracture is most commonly the neck of a femur or the region between the trochanters of a femur.

### Tibia

The **tibia,** or shin bone, is the larger of the two leg bones and is located on the medial side (fig. 7.31). Its proximal end is expanded into *medial* and *lateral condyles,* which have concave surfaces and articulate with the condyles of the femur. Below the condyles, on the anterior surface, is a process called the *tibial tuberosity,* which provides an attachment for the *patellar ligament*—a continuation of the patella-bearing tendon.

At its distal end, the tibia expands to form a prominence on the inner ankle called the *medial malleolus* (mah-le′o-lus), which is an attachment for ligaments. On its lateral side is a depression that articulates with the fibula. The inferior surface of the tibia's distal end articulates with a large bone (the talus) in the ankle.

### Fibula

The **fibula** is a long, slender bone located on the lateral side of the tibia (fig. 7.31). Its ends are slightly enlarged into a proximal *head* and a distal *lateral malleolus.* The head articulates with the tibia just below the lateral condyle; however, it does not enter into the knee joint and does not bear any body weight. The lateral malleolus articulates with the ankle and protrudes on the lateral side.

### Foot

The foot is made up of the ankle, the instep, and the toes. The ankle, or *tarsus* (tahr′sus), is composed of seven **tarsal bones** (figs. 7.32 and 7.33). These bones are arranged so that one of them, the **talus** (ta′lus), can move freely where it joins the tibia and fibula. The remaining tarsal bones are bound firmly together, forming a mass supporting the talus. Figure 7.33 names the individual bones of the tarsus.

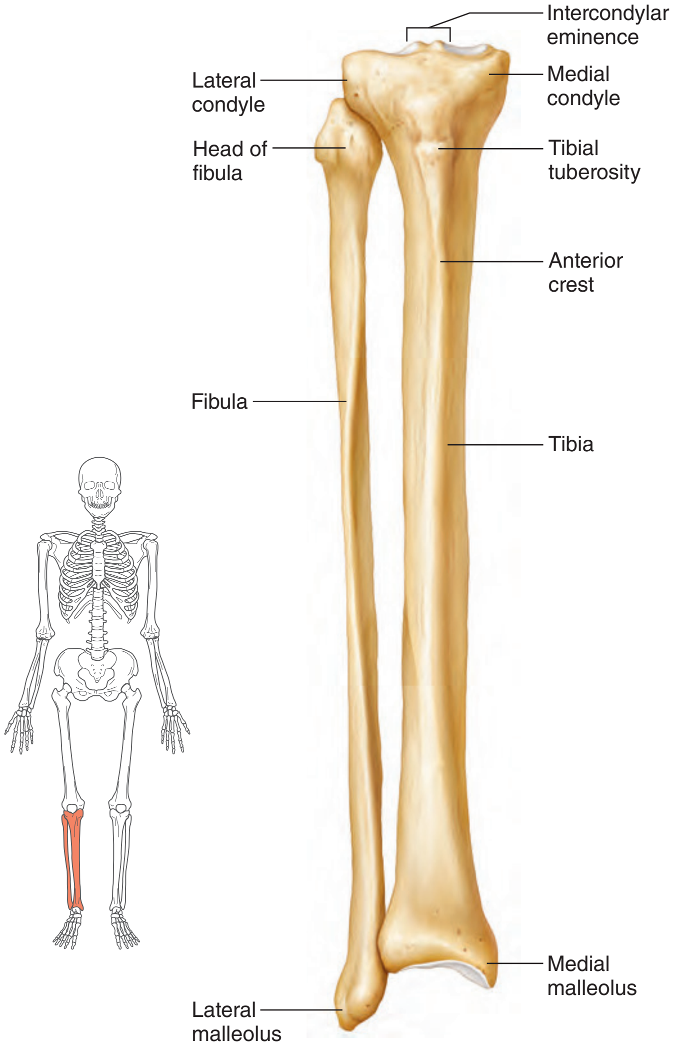

Intercondylar eminence
Lateral condyle
Medial condyle
Head of fibula
Tibial tuberosity
Anterior crest
Fibula
Tibia
Medial malleolus
Lateral malleolus

**FIGURE 7.31** APR Right tibia and fibula, anterior view.

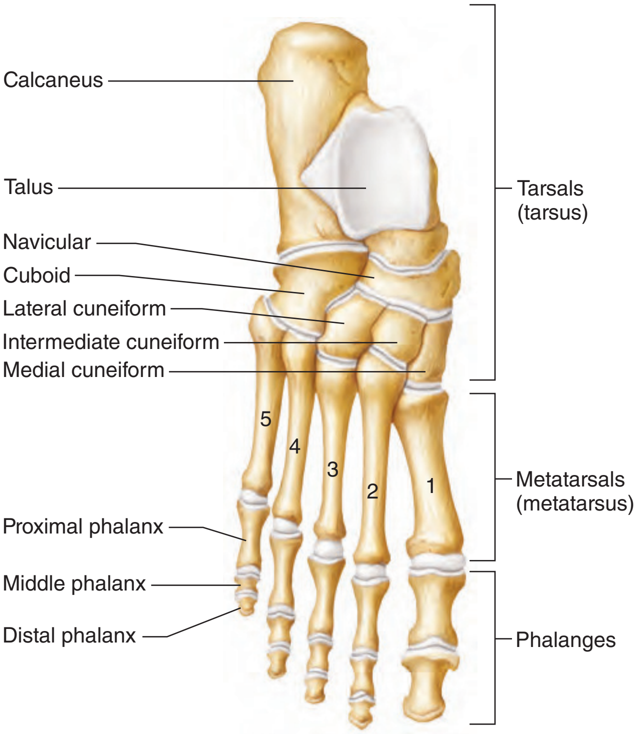

Calcaneus
Talus
Navicular
Cuboid
Lateral cuneiform
Intermediate cuneiform
Medial cuneiform
Tarsals (tarsus)
5
4
3
2
1
Metatarsals (metatarsus)
Proximal phalanx
Middle phalanx
Distal phalanx
Phalanges

**FIGURE 7.33** APR Right foot, viewed superiorly.

The largest of the tarsals, the **calcaneus** (kal-ka′ne-us), or heel bone, is below the talus, where it projects backward to form the base of the heel. The calcaneus helps support body weight and provides an attachment for the muscles that move the foot (see fig. 7.32).

The instep, or *metatarsus* (met″ah-tar′sus), consists of five elongated **metatarsal bones** that articulate with the tarsus. They are numbered 1–5, beginning on the medial side (fig. 7.33). The heads at the distal ends of these bones form the ball of the foot. The tarsals and metatarsals are arranged and bound by ligaments to form the arches of the foot. A longitudinal arch extends from the heel to the toe, and a transverse arch stretches across the foot. These arches provide a stable, springy

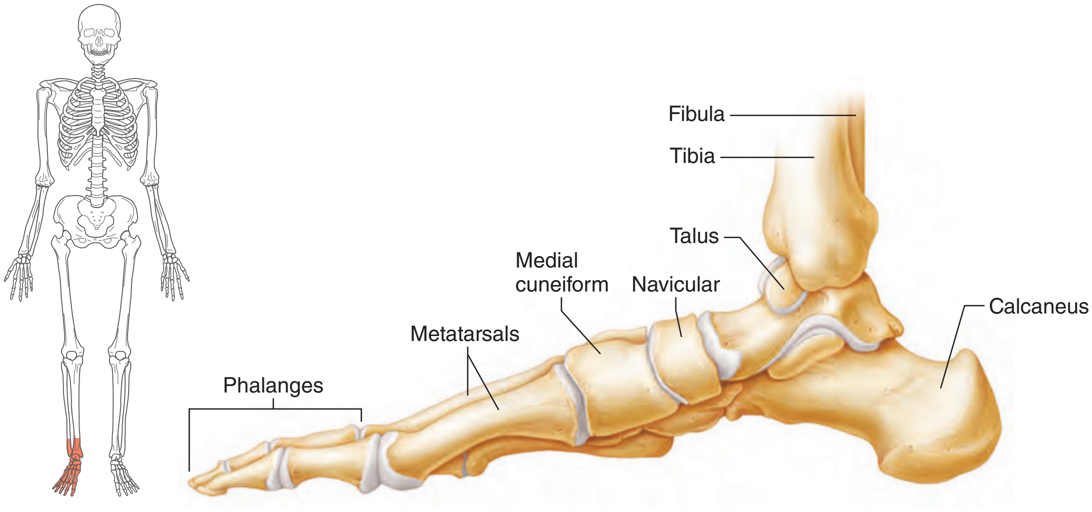

Fibula
Tibia
Talus
Medial cuneiform
Navicular
Calcaneus
Metatarsals
Phalanges

**FIGURE 7.32** Right foot, medial view. The talus moves freely where it articulates with the tibia and fibula.

base for the body. Sometimes, however, the tissues that bind the metatarsals weaken, producing fallen arches, or flat feet.

The **phalanges** of the toes, which are similar to those of the fingers, align and articulate with the metatarsals. Each toe has three phalanges—a proximal, a middle, and a distal phalanx—except the great toe, which has only a proximal and a distal phalanx, and lacks the middle phalanx.

**PRACTICE**

30. Locate and name each of the bones of the lower limb.
31. Explain how the bones of the lower limb articulate.
32. Describe how the foot is adapted to support the body.

## 7.13 | Joints

**Joints** (articulations) are functional junctions between bones. They bind parts of the skeletal system, make possible bone growth, permit parts of the skeleton to change shape during childbirth, and enable the body to move in response to skeletal muscle contractions. If classified according to the degree of movement they make possible, joints can be immovable (synarthrotic), slightly movable (amphiarthrotic), or freely movable (diarthrotic). Joints vary considerably in function and structure. Joints also can be grouped according to the type of tissue (fibrous, cartilaginous, or synovial) that binds the bones together at each junction. Currently, this structural classification by tissue type is most commonly used.

**FACTS OF LIFE** Typically an adult human body has 230 joints.

### Fibrous Joints

**Fibrous** (fi′brus) **joints** lie between bones that closely contact one another. A thin layer of dense connective tissue joins the bones at such joints, as in a *suture* between a pair of flat bones of the skull (fig. 7.34). Generally, no appreciable movement (synarthrotic) takes place at a fibrous joint. Some fibrous joints, such as the joint in the leg between the distal ends of the tibia and fibula, have limited movement (amphiarthrotic).

### Cartilaginous Joints

Hyaline cartilage, or fibrocartilage, connects the bones of **cartilaginous** (kar″tĭ-lah′jin-us) **joints.** For example, joints of this type separate the vertebrae of the vertebral column. Each intervertebral disc is composed of a band of fibrocartilage (annulus fibrosus) surrounding a pulpy or gelatinous core (nucleus pulposus). The disc absorbs shocks and helps equalize pressure between vertebrae when the body moves (see fig. 7.17).

Due to the slight flexibility of the discs, cartilaginous joints allow limited movement (amphiarthrotic), as when the back is bent forward or to the side or is twisted. Other examples of cartilaginous joints include the pubic symphysis and the first rib with the sternum.

### Synovial Joints APR

Most joints in the skeletal system are **synovial** (sĭ-no′ve-al) **joints,** which allow free movement (diarthrotic). They are more complex structurally than fibrous or cartilaginous joints.

The articular ends of the bones in a synovial joint are covered with a thin layer of hyaline cartilage (articular cartilage). A tubular *joint capsule,* composed of an outer fibrous layer of dense connective tissue and an inner lining of *synovial membrane,* which secretes *synovial fluid,* holds the bones of a synovial joint together (fig. 7.35). Ligaments in the fibrous layer prevent the bones from being pulled apart. Synovial fluid has a consistency similar to uncooked egg white, and it lubricates joints.

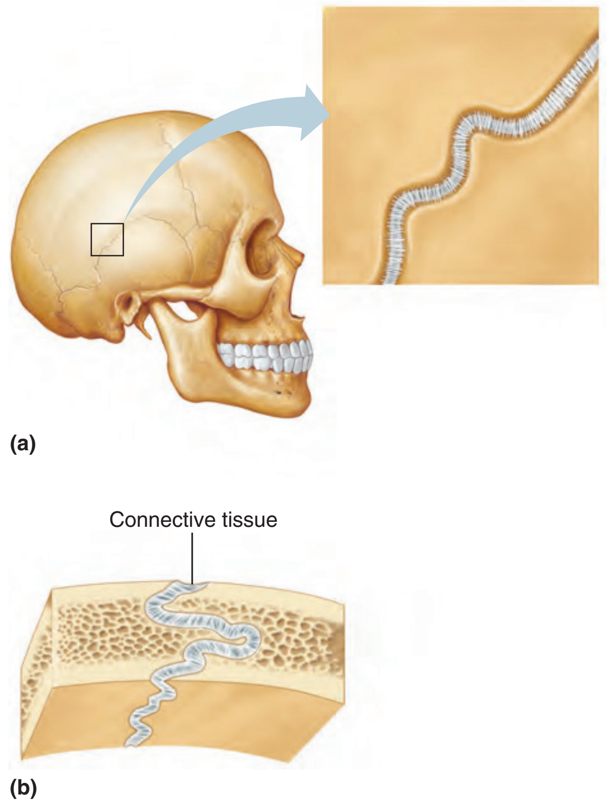


**FIGURE 7.34** Fibrous joints. **(a)** The fibrous joints between the bones of the skull are immovable and are called sutures. **(b)** A thin layer of connective tissue connects the bones at the suture.

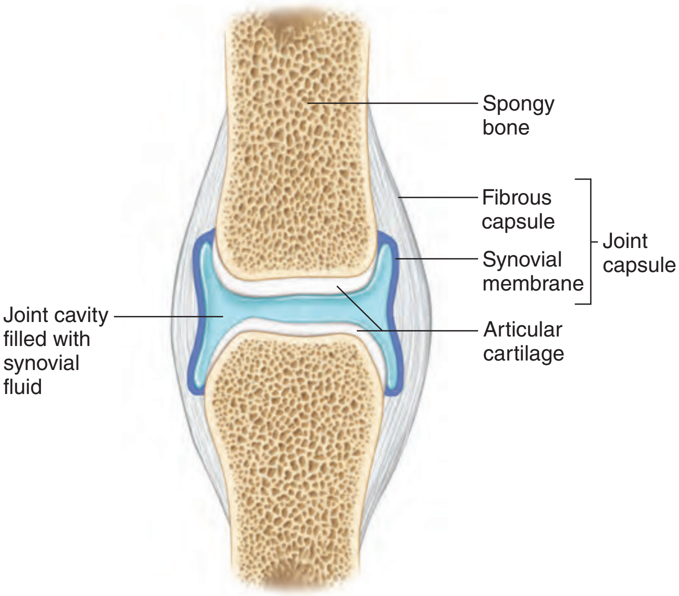


**FIGURE 7.35** The generalized structure of a synovial joint.

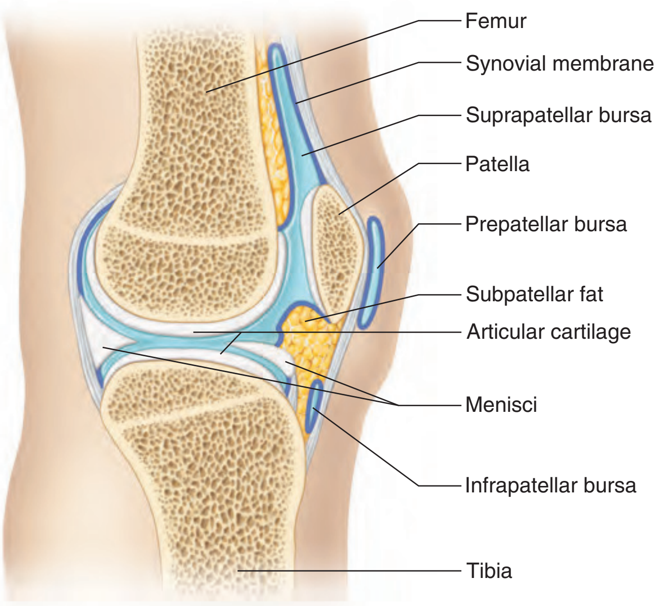


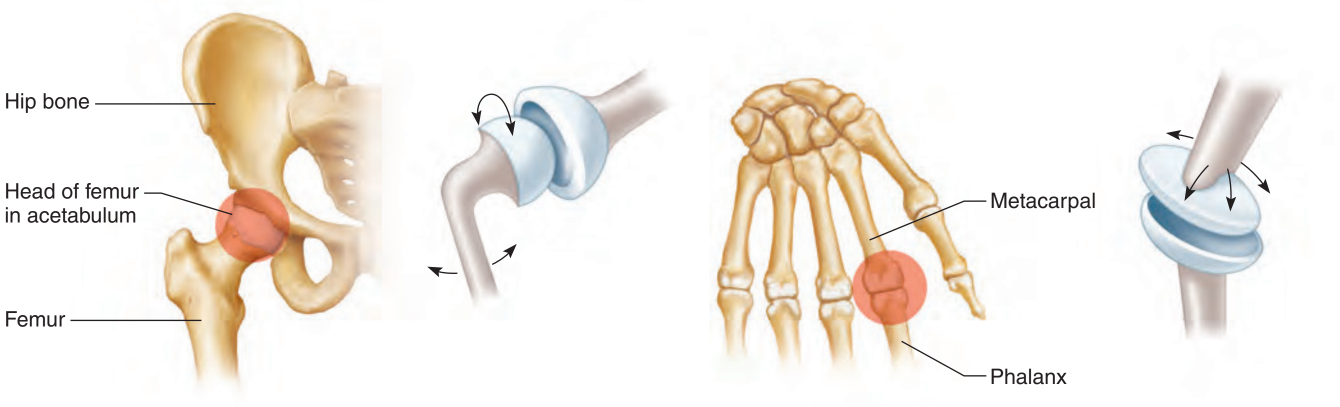
**FIGURE 7.36** Menisci separate the articulating surfaces of the femur and tibia. Several bursae are associated with the knee joint.

Some synovial joints have flattened, shock-absorbing pads of fibrocartilage called **menisci** (mĕ-nis′ke) (singular, *meniscus*) between the articulating surfaces of the bones (fig. 7.36). Such joints may also have fluid-filled sacs called **bursae** (ber′se) associated with them. Each bursa is lined with synovial membrane, which may be continuous with the synovial membrane of a nearby joint cavity. Bursae are commonly located between tendons and underlying bony prominences, as in the patella of the knee or the olecranon process of the elbow. They aid the movement of tendons that glide over these bony parts or over other tendons. Figure 7.36 shows and names some of the bursae associated with the knee.

Based upon the shapes of their parts and the movements they permit, synovial joints are classified as follows:

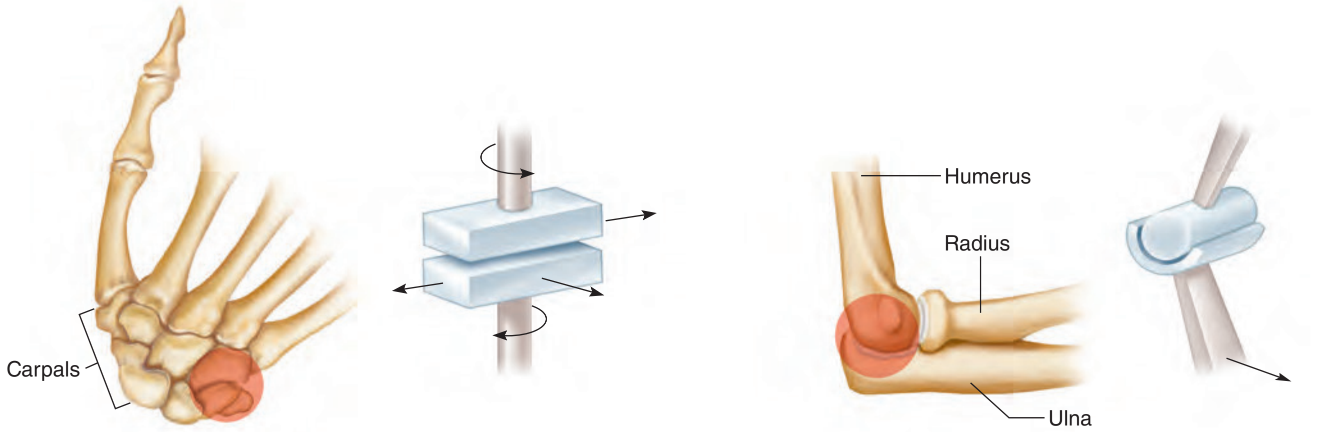
1. A **ball-and-socket joint,** or **spheroidal joint,** consists of a bone with a globular or slightly egg-shaped head that articulates with the cup-shaped cavity of another bone. Such a joint allows the widest range of motion, permitting movements in all planes (*multiaxial*), as well as rotational movement around a central axis. The shoulder and hip have joints of this type (fig. 7.37*a*).
2. In a **condylar joint,** or **ellipsoidal joint,** the ovoid condyle of one bone fits into the elliptical cavity of another bone, as in the joints between the metacarpals and phalanges (fig. 7.37*b*). This type of joint permits a variety of movements in different planes; rotational movement, however, is not possible.
3. The articulating surfaces of **plane joints,** or **gliding joints,** are nearly flat or slightly curved. Most of the joints in the wrist and ankle, as well as those between the articular processes of adjacent vertebrae, belong to this group (fig. 7.37*c*). They allow sliding and twisting movements. The sacroiliac joints and the joints formed by ribs 2–7 connecting with the sternum are also plane joints.
4. In a **hinge joint,** the convex surface of one bone fits into the concave surface of another, as in the elbow and the joints of the phalanges (fig. 7.37*d*). Such a joint resembles the hinge of a door in that it permits movement in one plane only (*uniaxial*).
5. In a **pivot joint,** or **trochoid joint,** the cylindrical surface of one bone rotates within a ring formed of bone and ligament. Movement is limited to the rotation around a central axis. The joint between the atlas and the dens of the axis is of this type (fig. 7.37*e*).
6. A **saddle joint,** or **sellar joint,** forms between bones whose articulating surfaces have both concave and convex regions. The surface of one bone fits the complementary surface of the other. This physical relationship permits a variety of movements, mainly in two planes (*biaxial*), as in the joint between the carpal (trapezium) and metacarpal of the thumb (fig. 7.37*f*).

Table 7.4 summarizes the types of joints. Clinical Application 7.2 discusses injuries and conditions that affect the joints.


Hip bone
Head of femur in acetabulum
Femur
Metacarpal
Phalanx

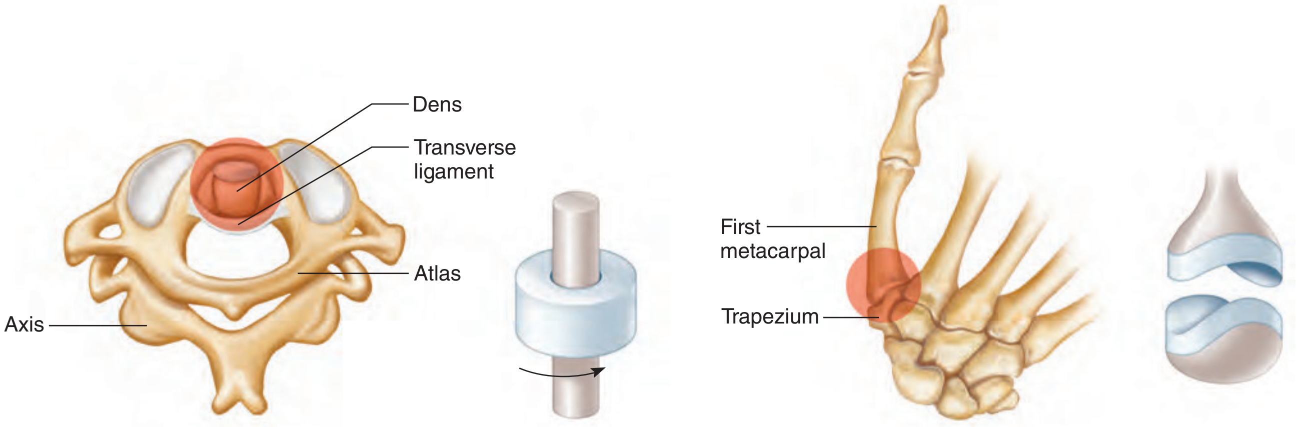
**(a)** Ball-and-socket joint

**(b)** Condylar joint


Carpals
Humerus
Radius
Ulna

**(c)** Plane joint

**(d)** Hinge joint


Dens
Transverse ligament
Atlas
Axis
First metacarpal
Trapezium

**(e)** Pivot joint

**(f)** Saddle joint

**FIGURE 7.37** APR Types and examples of synovial (freely movable) joints. **(a-f)**

## CLINICAL APPLICATION 7.2

## Joint Disorders

Joints must support weight, provide a variety of body movements, and are used frequently. Trauma, overuse, infection, a misdirected immune system attack, or degeneration can injure joints. Consider some common joint problems.

### Sprains

*Sprains* result from overstretching or tearing the connective tissues, including cartilage, ligaments, and tendons, associated with a joint, but they do not dislocate the articular bones. Usually a forceful wrenching or twisting sprains a wrist or ankle. For example, inverting an ankle too far can sprain it by stretching the ligaments on its lateral surface. Severe injuries may pull these structures loose from their attachments.

A sprained joint is painful and swollen, restricting movement. Immediate treatment of a sprain is rest; more serious cases require medical attention. However, immobilization of a joint, even for a brief period, causes bone resorption and weakens ligaments. Consequently, exercise may help strengthen the joint.

### Bursitis

Overuse of a joint or stress on a bursa may cause *bursitis,* an inflammation of a bursa. The bursa between the calcaneus (heel bone) and the Achilles tendon may become inflamed as a result of a sudden increase in physical activity using the feet. Bursitis is treated with rest. Medical attention may be necessary.

### Arthritis

*Arthritis* causes inflamed, swollen, and painful joints. More than a hundred different types of arthritis affect millions of people worldwide. The most common types of arthritis are rheumatoid arthritis (RA), osteoarthritis (OA), and Lyme arthritis.

#### Rheumatoid Arthritis (RA)

Rheumatoid arthritis, an autoimmune disorder (a condition in which the immune system attacks the body's healthy tissues), is painful and debilitating. The synovial membrane of a joint becomes inflamed and thickened. Then the articular cartilage is damaged, and fibrous tissue infiltrates, interfering with joint movements. Over time, the joints may ossify, fusing the articulating bones. RA may affect many joints or only a few. It is often accompanied by muscular atrophy, fatigue, and other symptoms.

#### Osteoarthritis (OA)

Osteoarthritis, a degenerative disorder, may result from aging or a poorly healed injury, or it may be inherited. Articular cartilage softens and disintegrates gradually, roughening the articular surfaces. Joints become painful, with restricted movement. OA usually affects the most active joints, such as those of the fingers, hips, knees, and the lower vertebral column.

If a person with osteoarthritis is overweight or obese, the first treatment is usually an exercise and dietary program to lose weight. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen have been used for many years to control osteoarthritis symptoms. NSAIDs called COX-2 inhibitors relieve inflammation without the gastrointestinal side effects of earlier drugs, but they are prescribed only to people who do not have risk factors for cardiovascular disease, to which some drugs are linked.

#### Lyme Arthritis

Lyme disease, a bacterial infection passed in a tick bite, causes intermittent arthritis of several joints, usually weeks after the initial symptoms of rash, fatigue, and flulike aches and pains. Lyme arthritis was first observed in Lyme, Connecticut, where an astute woman alerted a prominent rheumatologist to the fact that many of her young neighbors had what appeared to be the very rare juvenile form of rheumatoid arthritis. Researchers then traced the illness to a tick-borne bacterial infection. Antibiotic treatment that begins as soon as the early symptoms are recognized may prevent Lyme arthritis. Other types of bacteria can cause arthritis, too.

**TABLE 7.4 Types of Joints**

| Type of Joint | Description | Possible Movements | Examples |
|---|---|---|---|
| Fibrous | Articulating bones are fastened together by a thin layer of dense connective tissue. | None or slight twisting | Suture between bones of skull, joint between the distal ends of tibia and fibula |
| Cartilaginous | Articulating bones are connected by hyaline cartilage or fibrocartilage. | Limited movement, as when back is bent or twisted | Joints between the bodies of vertebrae, pubic symphysis |
| Synovial | Articulating ends of bones are surrounded by a joint capsule of ligaments and synovial membranes; ends of articulating bones are covered by hyaline cartilage and separated by synovial fluid. | Allow free movement (see the following list) | |
| Ball-and-socket | Ball-shaped head of one bone articulates with cup-shaped cavity of another. | Movements in all planes, including rotation | Shoulder, hip |
| Condylar | Oval-shaped condyle of one bone articulates with elliptical cavity of another. | Variety of movements in different planes, but no rotation | Joints between the metacarpals and phalanges |
| Plane | Articulating surfaces are nearly flat or slightly curved. | Sliding or twisting | Joints between various bones of wrist and ankle, sacroiliac joints, joints between ribs 2–7 and sternum |
| Hinge | Convex surface of one bone articulates with concave surface of another. | Flexion and extension | Elbow, joints of phalanges |
| Pivot | Cylindrical surface of one bone articulates with ring of bone and ligament. | Rotation around a central axis | Joint between the atlas and dens of the axis |
| Saddle | Articulating surfaces have both concave and convex regions; the surface of one bone fits the complementary surface of another. | Variety of movements, mainly in two planes | Joint between the carpal and metacarpal of thumb |

## Types of Joint Movements

Skeletal muscle action produces movements at synovial joints. Typically, one end of a muscle is attached to a less movable or relatively fixed part on one side of a joint, and the other end of the muscle is fastened to a more movable part on the other side. When the muscle contracts, its fibers pull its movable end (*insertion*) toward its fixed end (*origin*) and a movement occurs at the joint.

Note that in the anatomical position some actions have already occurred, such as supination of the forearm and hand, extension of the elbow, and extension of the knee. The muscle actions described in this section consider the entire range of movement at each joint, and do not necessarily presume that the starting point is the anatomical position. The following terms describe movements at joints (figs. 7.38, 7.39, and 7.40).

**flexion** (flek′shun) Bending parts at a joint so that the angle between them decreases and the parts come closer together (bending the knee).

**extension** (ek-sten′shun) Moving parts at a joint so that the angle between them increases and the parts move farther apart (straightening the knee).

**dorsiflexion** (dor″sĭ-flek′shun) Movement at the ankle that brings the foot closer to the shin (rocking back on one's heels).

**plantar flexion** (plan′tar flek′shun) Movement at the ankle that brings the foot farther from the shin (walking or standing on one's toes).

**hyperextension** (hi″per-ek-sten′shun) A term sometimes used to describe the extension of the parts at a joint beyond the anatomical position (bending the head back beyond the upright position); often used to describe an abnormal extension beyond the normal range of motion, resulting in injury.

**abduction** (ab-duk′shun) Moving a part away from the midline (lifting the upper limb horizontally to form a right angle with the side of the body). Abduction of the head and neck and bending of the trunk to the side may be termed *lateral flexion*.

**adduction** (ah-duk′shun) Moving a part toward the midline (returning the upper limb from the horizontal position to the side of the body).

**rotation** (ro-ta′shun) Moving a part around an axis (twisting the head from side to side).

**circumduction** (ser″kum-duk′shun) Moving a part so that its end follows a circular path (moving the finger in a circular motion without moving the hand).

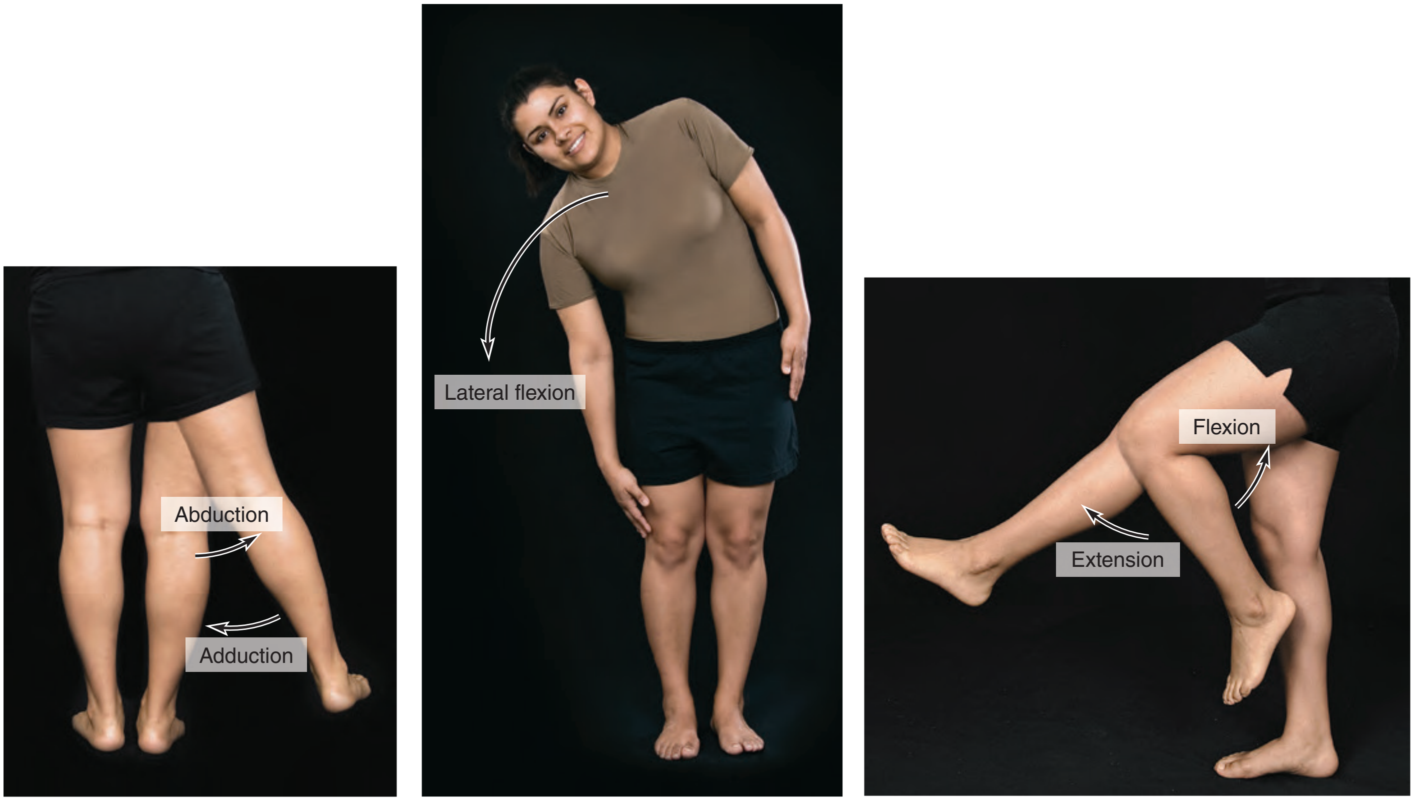

Abduction
Adduction
Lateral flexion
Flexion
Extension

**FIGURE 7.38** APR Joint movements illustrating abduction, adduction, lateral flexion, extension, and flexion.

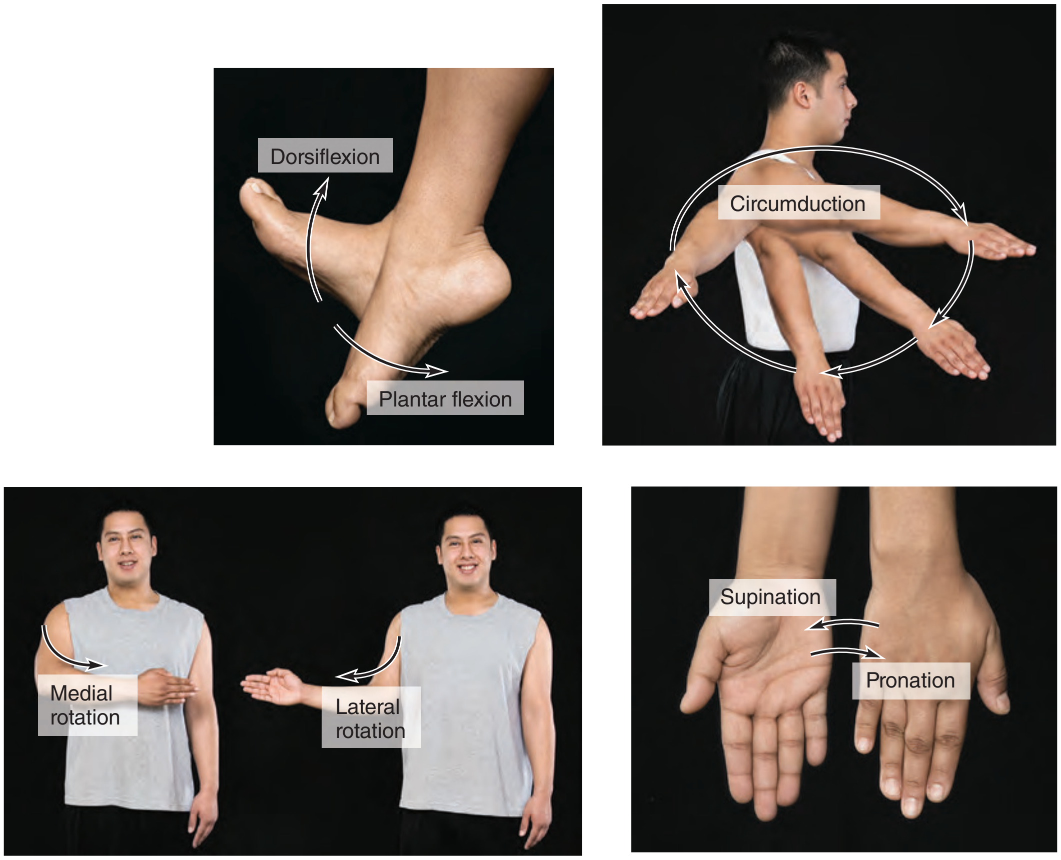

Dorsiflexion
Plantar flexion
Circumduction
Medial rotation
Lateral rotation
Supination
Pronation

**FIGURE 7.39** APR Joint movements illustrating dorsiflexion, plantar flexion, circumduction, rotation, supination, and pronation.

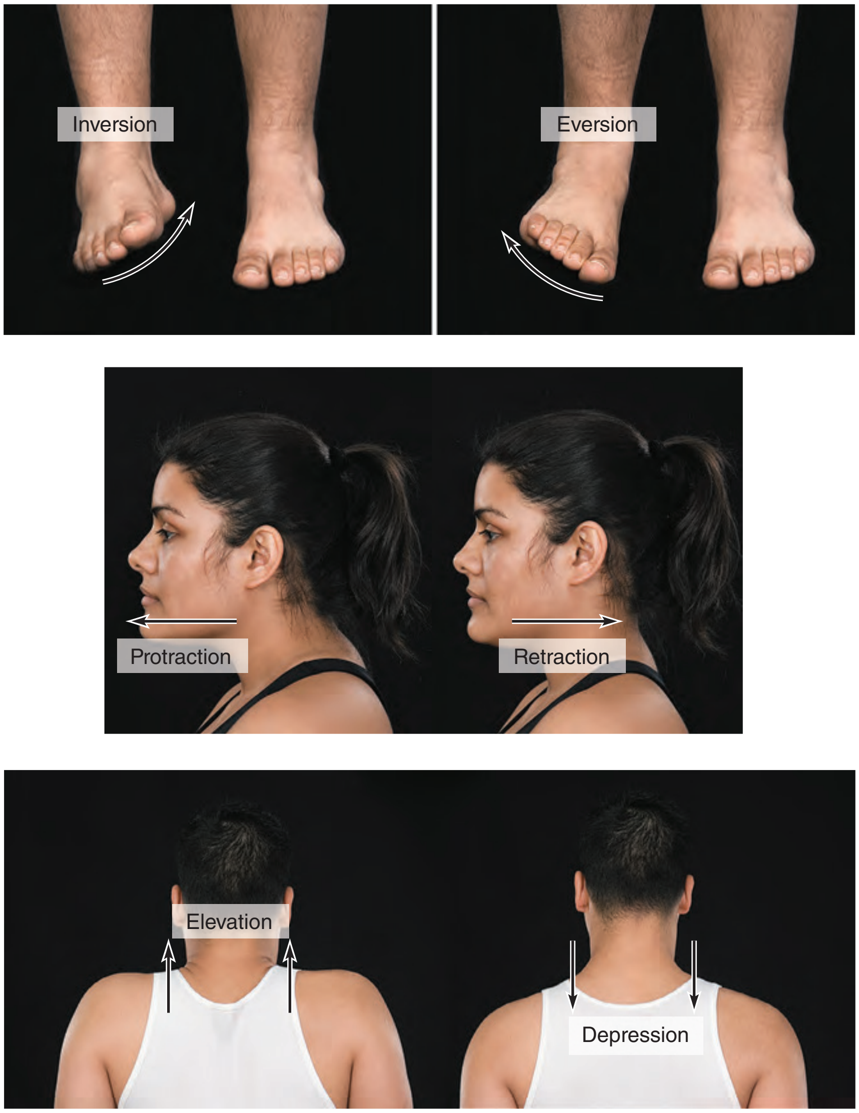


**FIGURE 7.40** AP|R Joint movements illustrating inversion, eversion, protraction, retraction, elevation, and depression.

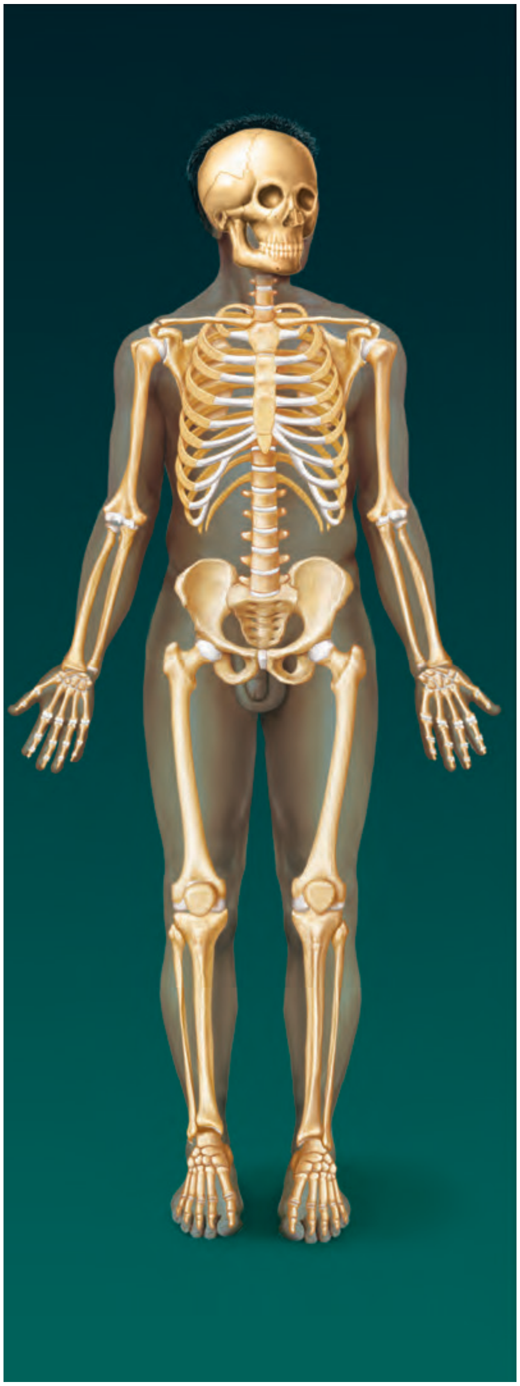
**pronation** (pro-na′shun) Rotation of the forearm so the palm is downward or facing posteriorly (in anatomical position).
**supination** (soo″pĭ-na′shun) Rotation of the forearm so the palm is upward or facing anteriorly (in anatomical position).
**eversion** (e-ver′zhun) Turning the foot so the plantar surface faces laterally.
**inversion** (in-ver′zhun) Turning the foot so the plantar surface faces medially.
**retraction** (re-trak′shun) Moving a part backward (pulling the head backward).
**protraction** (pro-trak′shun) Moving a part forward (thrusting the head forward).
**elevation** (el″ĕ-va′shun) Raising a part (shrugging the shoulders).
**depression** (de-presh′un) Lowering a part (drooping the shoulders).

## PRACTICE

33. Describe the characteristics of the three major types of joints.
34. Name six types of synovial joints.
35. What terms describe movements possible at synovial joints?

Injuries to the elbow, shoulder, and knee are commonly diagnosed and treated using a procedure called *arthroscopy*. Arthroscopy enables a surgeon to visualize the interior of a joint and perform diagnostic or therapeutic procedures, guided by the image on a video screen. An arthroscope is a thin, tubular instrument about 25 centimeters long containing optical fibers that transmit an image. The surgeon inserts the device through a small incision in the joint capsule. Arthroscopy is far less invasive than conventional surgery. Many runners have undergone uncomplicated arthroscopy and raced just weeks later.

# Skeletal System



Bones provide support, protection, and movement and also play a role in calcium balance.

## Integumentary System

Vitamin D, production of which begins in the skin, plays a role in calcium absorption and availability for bone matrix.

## Lymphatic System

Cells of the immune system originate in the bone marrow.

## Muscular System

Muscles pull on bones to cause movement.

## Digestive System

Absorption of dietary calcium provides material for bone matrix.

## Nervous System

Proprioceptors sense the position of body parts. Pain receptors warn of trauma to bone. Bones protect the brain and spinal cord.

## Respiratory System

Ribs and muscles work together in breathing.

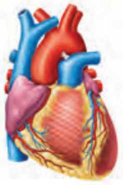
## Endocrine System

Some hormones act on bone to help regulate blood calcium levels.

## Urinary System

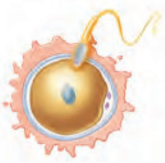
The kidneys and bones work together to help regulate blood calcium levels.

## Cardiovascular System



Blood transports nutrients to bone cells. Bone helps regulate plasma calcium levels, important to heart function.

## Reproductive System



The pelvis helps support the uterus during pregnancy. Bones provide a source of calcium during lactation.

# Summary Outline

### 7.1 Introduction (p. 144)

*Individual bones are the organs of the skeletal system. A bone contains active tissues.*

### 7.2 Bone Structure (p. 144)

*Bone structure reflects its function.*

1. Bones are classified according to their shapes—long, short, flat, or irregular.
2. Parts of a long bone
    a. Epiphyses at each end are covered with articular cartilage and articulate with other bones.
    b. The shaft of a bone is called the diaphysis.
    c. Except for the articular cartilage, a bone is covered by a periosteum.
    d. Compact bone has a continuous extracellular matrix with no gaps.
    e. Spongy bone has irregular interconnecting spaces between bony plates, trabeculae, that reduce the weight of bone.
    f. Both compact and spongy bone are strong and resist bending.
    g. The diaphysis contains a medullary cavity filled with marrow.
3. Microscopic structure
    a. Compact bone contains osteons cemented together.
    b. Central canals contain blood vessels that nourish the cells of osteons.
    c. Diffusion from the surface of the thin, bony plates nourishes the cells of spongy bone.

### 7.3 Bone Development and Growth (p. 146)

1. Intramembranous bones
    a. Intramembranous bones develop from sheetlike layers of unspecialized connective tissues.
    b. Osteoblasts within the membranous layers form bone tissue.
    c. Mature bone cells are called osteocytes.
2. Endochondral bones
    a. Endochondral bones develop as hyaline cartilage that is later replaced by bone tissue.
    b. The primary ossification center appears in the diaphysis, whereas secondary ossification centers appear in the epiphyses.
    c. An epiphyseal plate remains between the primary and secondary ossification centers.
    d. The epiphyseal plates are responsible for lengthening.
    e. Long bones continue to lengthen until the epiphyseal plates are ossified.
    f. Growth in thickness is due to ossification beneath the periosteum.
3. Homeostasis of bone tissue
    a. Osteoclasts break down bone matrix, and osteoblasts deposit bone matrix to continually remodel bone.
    b. The total mass of bone remains nearly constant.
4. Factors affecting bone development, growth, and repair include nutrition, hormonal secretions, and physical exercise.

### 7.4 Bone Function (p. 148)

1. Support and protection
    a. Bones shape and form body structures.
    b. Bones support and protect softer underlying tissues.
2. Body movement
    a. Bones and muscles function together as levers.
    b. A lever consists of a bar, a pivot (fulcrum), a resistance, and a force that supplies energy.
3. Blood cell formation
    a. At different ages, hematopoiesis occurs in the yolk sac, liver and spleen, and red bone marrow.
    b. Red marrow houses developing red blood cells, white blood cells, and blood platelets. Yellow marrow stores fat.
4. Storage of inorganic salts
    a. Bones store calcium in the extracellular matrix of bone tissue, which contains large quantities of calcium phosphate.
    b. When blood calcium is low, osteoclasts break down bone, releasing calcium salts. When blood calcium is high, osteoblasts form bone tissue and store calcium salts.
    c. Bone stores small amounts of magnesium, sodium, potassium, and carbonate ions.

### 7.5 Skeletal Organization (p. 153)

1. The skeleton can be divided into axial and appendicular portions.
2. The axial skeleton consists of the skull, hyoid bone, vertebral column, and thoracic cage.
3. The appendicular skeleton consists of the pectoral girdle, upper limbs, pelvic girdle, and lower limbs.

### 7.6 Skull (p. 155)

*The skull consists of twenty-two bones: eight cranial bones and fourteen facial bones.*

1. Cranium
    a. The cranium encloses and protects the brain.
    b. Some cranial bones contain air-filled paranasal sinuses.
    c. Cranial bones include the frontal bone, parietal bones, occipital bone, temporal bones, sphenoid bone, and ethmoid bone.
2. Facial skeleton
    a. Facial bones form the basic shape of the face and provide attachments for muscles.
    b. Facial bones include the maxillae, palatine bones, zygomatic bones, lacrimal bones, nasal bones, vomer bone, inferior nasal conchae, and mandible.
3. Infantile skull
    a. Fontanels connect incompletely developed bones.
    b. The proportions of the infantile skull are different from those of an adult skull.

### 7.7 Vertebral Column (p. 160)

*The vertebral column extends from the skull to the pelvis and protects the spinal cord. It is composed of vertebrae separated by intervertebral discs.*

1. A typical vertebra
    a. A typical vertebra consists of a body and a bony vertebral arch, which surrounds the spinal cord.
    b. Notches on the upper and lower surfaces provide intervertebral foramina through which spinal nerves pass.
2. Cervical vertebrae
    a. Transverse processes bear transverse foramina.
    b. The atlas (first vertebra) supports and balances the head.
    c. The dens of the axis (second vertebra) provides a pivot for the atlas when the head is turned from side to side.
3. Thoracic vertebrae
    a. Thoracic vertebrae are larger than cervical vertebrae.
    b. Facets on the sides articulate with the ribs.
4. Lumbar vertebrae
    a. The vertebral bodies are large and strong.
    b. They support more body weight than other vertebrae.
5. Sacrum
    a. The sacrum is a triangular structure formed of five fused vertebrae.
    b. Vertebral foramina form the sacral canal.
6. Coccyx
    a. The coccyx, composed of four fused vertebrae, forms the lowest part of the vertebral column.
    b. It acts as a shock absorber when a person sits.

### 7.8 Thoracic Cage (p. 164)

*The thoracic cage includes the ribs, thoracic vertebrae, sternum, and costal cartilages. It supports the pectoral girdle and upper limbs, protects viscera, and functions in breathing.*

1. Ribs
    a. Twelve pairs of ribs attach to the twelve thoracic vertebrae.
    b. Costal cartilages of the true ribs join the sternum directly. Those of the false ribs join it indirectly or not at all.
    c. A typical rib has a shaft, a head, and tubercles that articulate with the vertebrae.
2. Sternum
    a. The sternum consists of a manubrium, body, and xiphoid process.
    b. It articulates with the clavicles.

### 7.9 Pectoral Girdle (p. 164)

*The pectoral girdle is composed of two clavicles and two scapulae. It forms an incomplete ring that supports the upper limbs and provides attachments for muscles that move the upper limbs.*

1. Clavicles
    a. Clavicles are rodlike bones located between the sternum and the scapulae.
    b. They hold the shoulders in place and provide attachments for muscles.
2. Scapulae
    a. The scapulae are broad, triangular bones.
    b. They articulate with the humerus of each upper limb and provide attachments for muscles of the upper limbs and chest.

### 7.10 Upper Limb (p. 166)

*Bones of the upper limb form the framework, provide the attachments for muscles, and function in levers that move the limb and its parts.*

1. Humerus
    a. The humerus extends from the scapula to the elbow.
    b. It articulates with the radius and ulna at the elbow.
2. Radius
    a. The radius is located on the thumb side of the forearm between the elbow and the wrist.
    b. It articulates with the humerus, ulna, and wrist.
3. Ulna
    a. The ulna is longer than the radius and overlaps the humerus posteriorly.
    b. It articulates with the radius laterally and with a disc of fibrocartilage inferiorly.
4. Hand
    a. The wrist is composed of eight carpal bones that form a carpus.
    b. The palm or metacarpus includes five metacarpal bones and fourteen phalanges compose the fingers.

### 7.11 Pelvic Girdle (p. 168)

*The pelvic girdle consists of two hip bones that articulate with each other anteriorly and with the sacrum posteriorly.*

1. The sacrum, coccyx, and pelvic girdle form the bowl-shaped pelvis.
2. Each hip bone consists of an ilium, ischium, and pubis, which are fused in the region of the acetabulum.
    a. The ilium
        (1) The ilium is the largest portion of the hip bone.
        (2) It joins the sacrum at the sacroiliac joint.
    b. The ischium
        (1) The ischium is the lowest portion of the hip bone.
        (2) It supports the body weight when sitting.
    c. The pubis
        (1) The pubis is the anterior portion of the hip bone.
        (2) The pubic bones are joined anteriorly at the pubic symphysis.

### 7.12 Lower Limb (p. 172)

*Bones of the lower limb provide a framework for the lower limb and provide attachments for muscles that move the lower limb.*

1. Femur
    a. The femur extends from the hip to the knee.
    b. The patella articulates with the femur's anterior surface.
2. Tibia
    a. The tibia is located on the medial side of the leg.
    b. It articulates proximally with the femur and distally with the talus of the ankle.
3. Fibula
    a. The fibula is located on the lateral side of the tibia.
    b. It articulates proximally with the tibia and distally with the ankle. It does not bear body weight.
4. Foot
    a. The ankle consists of the tarsus formed by the talus and six other tarsals.
    b. The instep or metatarsus includes five metatarsals, and fourteen phalanges compose the toes.

### 7.13 Joints (p. 174)

*Joints can be classified according to degree of movement as well as according to the type of tissue that binds the bones together.*

1. Fibrous joints
    a. Bones at fibrous joints are tightly joined by a layer of dense connective tissue.
    b. Limited movement (amphiarthrotic) or no movement (synarthrotic) occurs at a fibrous joint.
2. Cartilaginous joints
    a. A layer of cartilage joins the bones of cartilaginous joints.
    b. Such joints allow limited movement (amphiarthrotic).
3. Synovial joints
    a. The bones of a synovial joint are covered with hyaline cartilage and held together by a fibrous joint capsule.
    b. The joint capsule consists of an outer layer of ligaments and an inner lining of synovial membrane.
    c. Pads of fibrocartilage, menisci, act as shock absorbers in some synovial joints.
    d. Bursae are located between tendons and underlying bony prominences.
    e. Synovial joints that allow free movement (diarthrotic) include ball-and-socket, condylar, plane, hinge, pivot, and saddle.
4. Types of joint movements
    a. Muscles fastened on either side of a joint produce the movements of synovial joints.
    b. Joint movements include flexion, extension, dorsiflexion, plantar flexion, hyperextension, abduction, adduction, rotation, circumduction, pronation, supination, eversion, inversion, retraction, protraction, elevation, and depression.

## CHAPTER ASSESSMENTS

### 7.1 Introduction

**1.** Active, living tissues found in bone include ___________. (p. 144)

a. blood
b. nervous tissue
c. bone tissue
d. all of the above

### 7.2 Bone Structure

**2.** Sketch a typical long bone, and label its epiphyses, diaphysis, medullary cavity, periosteum, and articular cartilages. On the sketch, designate the locations of compact and spongy bone. (pp. 144–145)

**3.** Discuss the functions of the parts labeled in the sketch you made for question 2. (pp. 144–145)

**4.** Distinguish between the microscopic structure of compact bone and spongy bone. (pp. 145–146)

### 7.3 Bone Development and Growth

**5.** Explain how the development of intramembranous bone differs from that of endochondral bone. (p. 147)

**6.** ________ are mature bone cells, whereas ________ are bone-forming cells and ________ are bone-resorbing cells. (pp. 147–148)

**7.** Explain the function of an epiphyseal plate. (p. 148)

**8.** Physical exercise pulling on muscular attachments to bones stimulates ____________. (p. 148)

### 7.4 Bone Function

**9.** Give several examples of how bones support and protect body parts. (p. 149)

**10.** List and describe other functions of bones. (p. 149)

### 7.5 Skeletal Organization

**11.** Bones of the head, neck, and trunk compose the ____________ skeleton; bones of the limbs and their attachments compose the ____________ skeleton. (p. 153)

### 7.6–7.12 (Skull–Lower Limb)

**12.** Name the bones of the cranium and the facial skeleton. (pp. 155–160)

**13.** Describe a typical vertebra, and distinguish among the cervical, thoracic, and lumbar vertebrae. (pp. 160–162)

**14.** Name the bones that compose the thoracic cage. (p. 164)

**15.** The clavicle and scapula form the ______________ girdle, whereas the hip bones form the ______________ girdle. (pp. 164 and 166)

**16.** Name the bones of the upper and lower limbs. (pp. 166–174)

**17.** Match the parts listed on the left with the bones listed on the right. (pp. 155–174)

(1) foramen magnum
(2) mastoid process
(3) palatine process
(4) sella turcica
(5) deltoid tuberosity
(6) greater trochanter
(7) lateral malleolus
(8) medial malleolus
(9) radial tuberosity
(10) xiphoid process

A. maxilla
B. occipital bone
C. temporal bone
D. femur
E. fibula
F. humerus
G. radius
H. sternum
I. tibia
J. sphenoid bone

### 7.13 Joints

**18.** Describe and give an example of a fibrous joint, a cartilaginous joint, and a synovial joint. (p. 174)

**19.** Name an example of each type of synovial joint, and describe the parts of the joint as they relate to the movement(s) allowed by that particular joint. (p. 175)

**20.** Joint movements occur when a muscle contracts and the muscle fibers pull the muscle's movable end of attachment to the bone, the _______, toward its fixed end, the _______. (p. 178)

**21.** Match the movement on the left with the appropriate description on the right. (pp. 178–180)

(1) rotation
(2) supination
(3) extension
(4) eversion
(5) protraction
(6) flexion
(7) pronation
(8) abduction
(9) depression
(10) adduction

A. turning the palm upward
B. decreasing the angle between parts
C. moving a part forward
D. moving a part around axis
E. moving a part toward midline
F. turning the foot so plantar surface faces laterally
G. increasing the angle between parts
H. lowering a part
I. turning the palm downward
J. moving a part away from midline

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 5.3, 7.2, 7.6

**1.** How does the structure of a bone make it strong yet lightweight?

### OUTCOMES 5.3, 7.13

**2.** How would you explain to an athlete why damaged joint ligaments and cartilages are so slow to heal following an injury?

### OUTCOMES 7.3, 7.4, 7.10, 7.12

**3.** When a child's bone is fractured, growth may be stimulated at the epiphyseal plate of that bone. What problems might this extra growth cause in an upper or lower limb before the growth of the other limb compensates for the difference in length?

### OUTCOMES 7.3, 7.4, 7.11

**4.** Suppose archaeologists discover human skeletal remains in Ethiopia. Examination of the bones suggests that the remains represent four types of individuals. Two of the skeletons have bone densities that are 30% less than those of the other two skeletons. The skeletons with the lower bone mass also have broader front pelvic bones. Within the two groups defined by bone mass, smaller skeletons have bones with evidence of epiphyseal plates, but larger bones have only a thin line where the epiphyseal plates should be. Give the age group and gender of the individuals in this find.

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# HUMAN SKULL

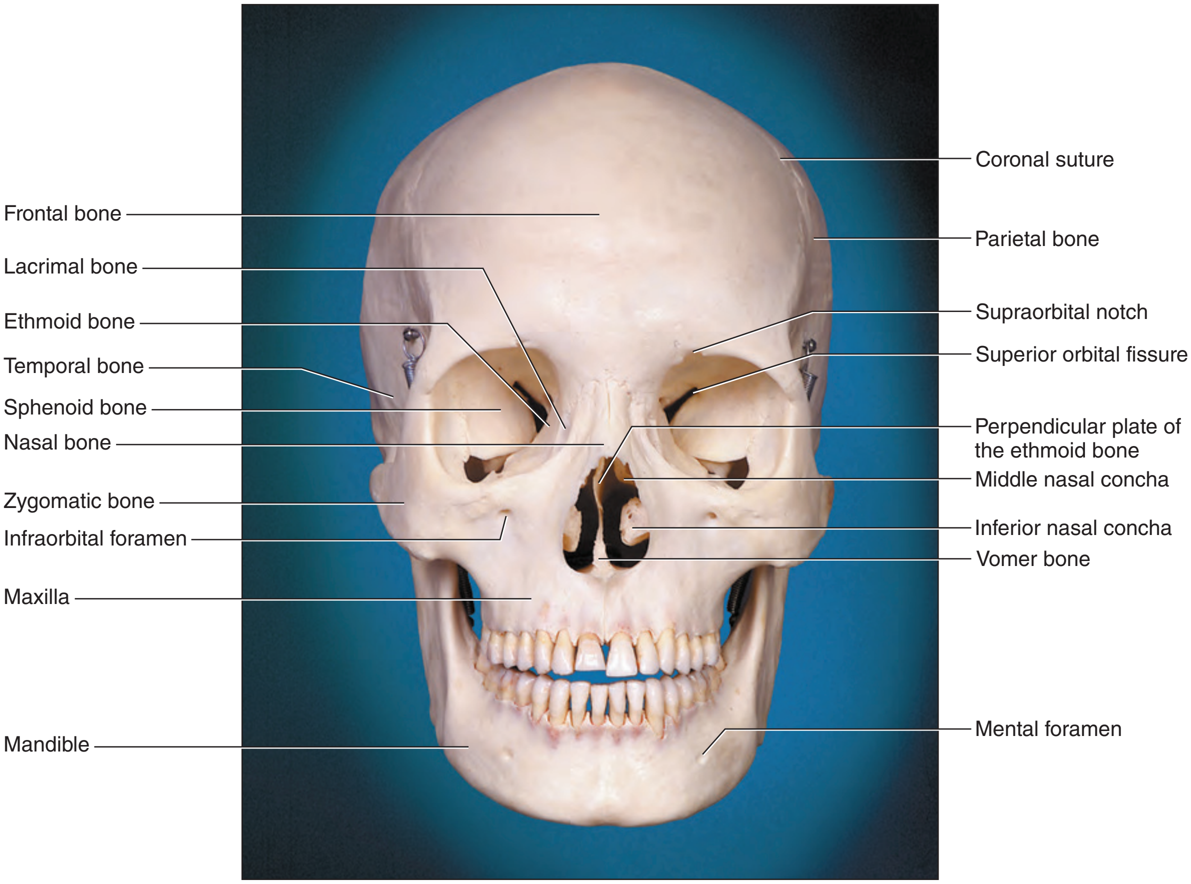

Frontal bone
Lacrimal bone
Ethmoid bone
Temporal bone
Sphenoid bone
Nasal bone
Zygomatic bone
Infraorbital foramen
Maxilla
Mandible
Coronal suture
Parietal bone
Supraorbital notch
Superior orbital fissure
Perpendicular plate of the ethmoid bone
Middle nasal concha
Inferior nasal concha
Vomer bone
Mental foramen

**PLATE EIGHT** The skull, anterior view.

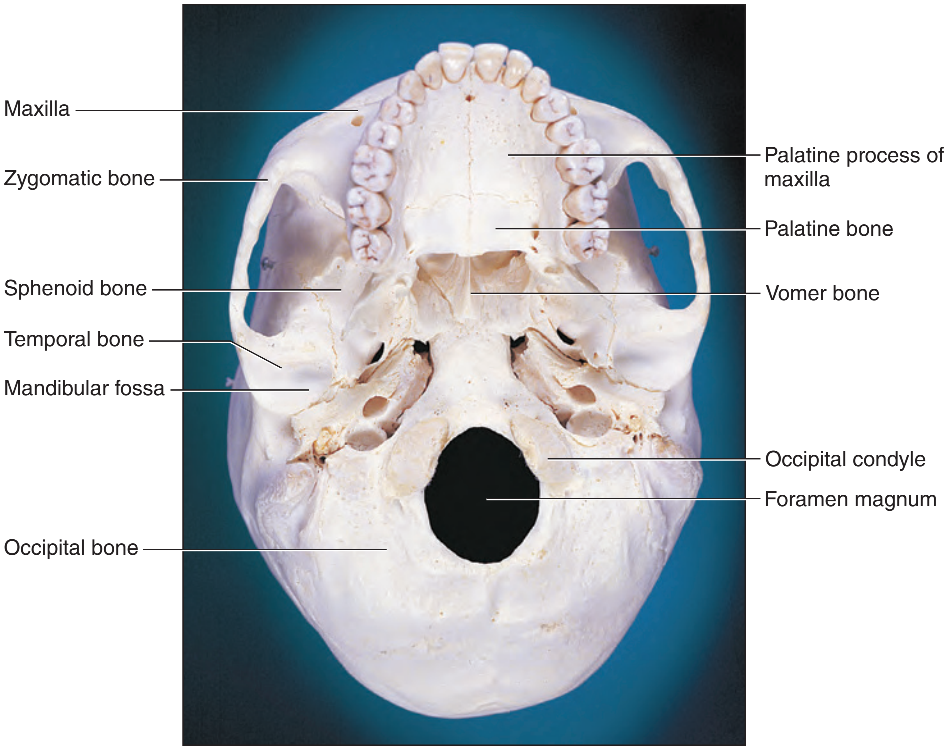

Maxilla
Zygomatic bone
Sphenoid bone
Temporal bone
Mandibular fossa
Occipital bone
Palatine process of maxilla
Palatine bone
Vomer bone
Occipital condyle
Foramen magnum

**PLATE NINE** The skull, inferior view.

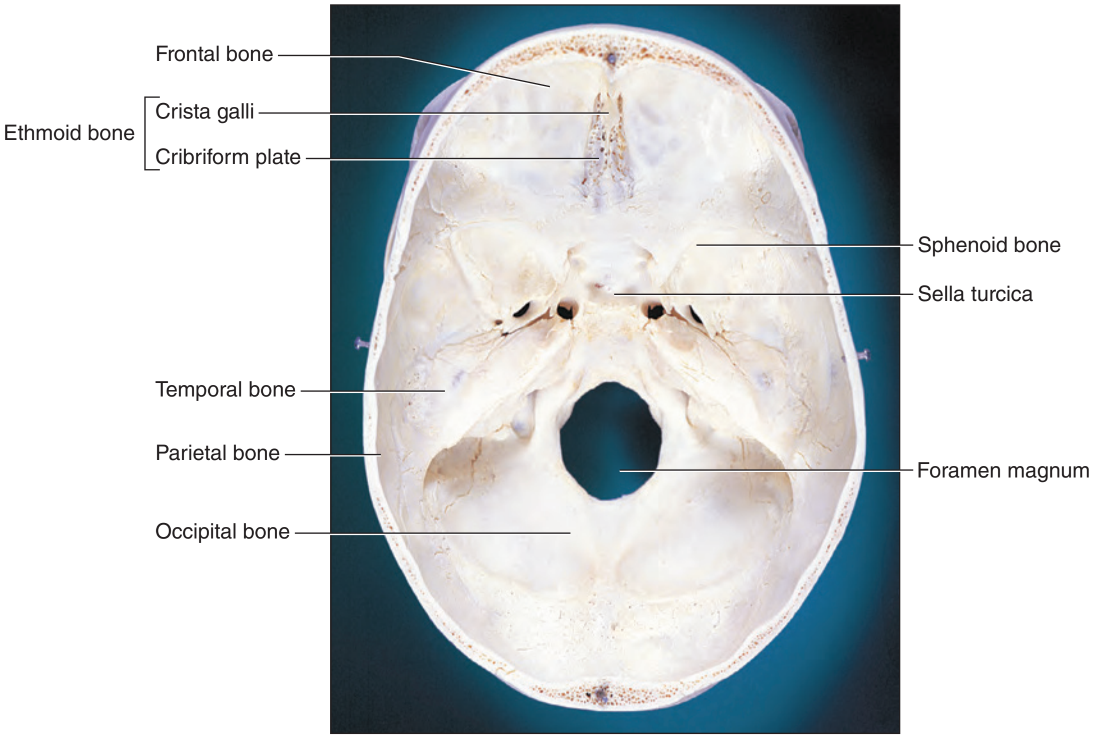

Frontal bone
Ethmoid bone
Crista galli
Cribriform plate
Temporal bone
Parietal bone
Occipital bone
Sphenoid bone
Sella turcica
Foramen magnum

**PLATE TEN** The skull, floor of the cranial cavity.

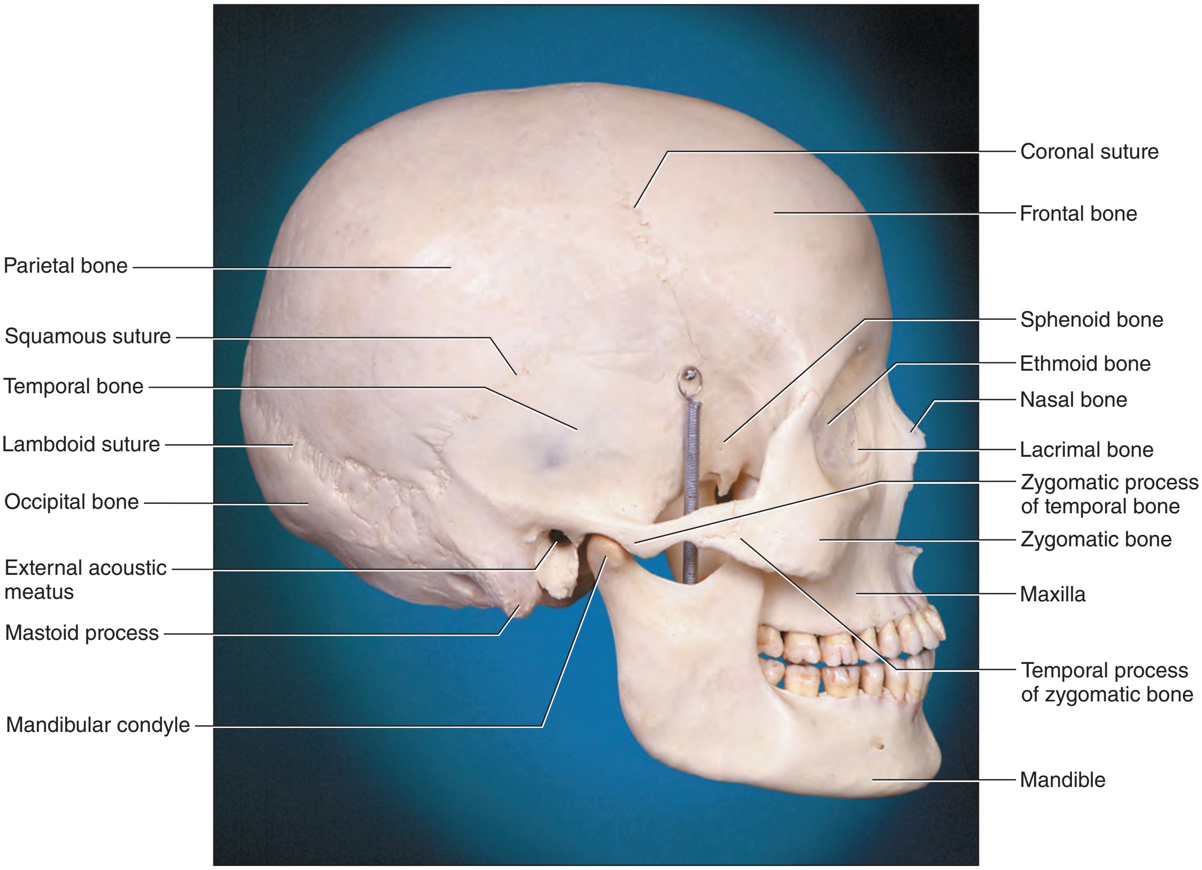

Coronal suture
Frontal bone
Parietal bone
Squamous suture
Temporal bone
Lambdoid suture
Occipital bone
External acoustic meatus
Mastoid process
Mandibular condyle
Sphenoid bone
Ethmoid bone
Nasal bone
Lacrimal bone
Zygomatic process of temporal bone
Zygomatic bone
Maxilla
Temporal process of zygomatic bone
Mandible

**PLATE ELEVEN** The skull, right lateral view.

# 8

# Muscular System

Regular resistance training (weight training) can strengthen muscles.

Double the muscle. The newborn had an astonishing appearance—his prominent arm and thigh muscles looked as if he'd been weightlifting in the womb. When the child reached five years of age, his muscles were twice normal size, and he could lift weights heavier than many adults could lift. He also had half the normal amount of body fat.

The boy's muscle cells cannot produce a protein called myostatin, which normally stops stem cells from developing into muscle cells. In this boy a mutation turned off this genetic brake, and as a result his muscles bulge, their cells both larger and more numerous than those in the muscles of an unaffected child. The boy is healthy so far, but because myostatin is also normally made in cardiac muscle, he may develop heart problems.

Other species with myostatin mutations are well known. Naturally "double-muscled" cattle and sheep are valued for their high weights early in life. Chicken breeders lower myostatin production to yield meatier birds, and "mighty mice" with silenced myostatin genes are used in basic research to study muscle overgrowth. In clinical applications, researchers are investigating ways to block myostatin activity to stimulate muscle growth to reverse muscle-wasting from AIDS, cancer, and muscular dystrophy. Myostatin could also be abused to enhance athletic performance.

Apart from double-muscle mutations, resistance (weight) training can increase the ratio of muscle to fat in our bodies, which offers several benefits. Because muscle cells burn calories at three times the rate of fat cells, a lean body is more energetically efficient. Weight training increases muscle strength and bone density; lowers blood pressure; decreases the risks of developing arthritis, osteoporosis, and diabetes mellitus; and is even associated with improved self-esteem and fewer sick days.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

**8.1 Introduction**

1. List various outcomes of muscle actions. (p. 189)

**8.2 Structure of a Skeletal Muscle**

2. Identify the structures that make up a skeletal muscle. (p. 189)
3. Identify the major parts of a skeletal muscle fiber, and the function of each. (p. 190)
4. Discuss nervous stimulation of a skeletal muscle. (p. 192)

**8.3 Skeletal Muscle Contraction**

5. Identify the major events of skeletal muscle fiber contraction. (pp. 193–195)
6. List the energy sources for muscle fiber contraction. (p. 195)
7. Describe how oxygen debt develops. (p. 196)
8. Describe how a muscle may become fatigued. (p. 197)

**8.4 Muscular Responses**

9. Distinguish among a twitch, recruitment, and a sustained contraction. (pp. 198–200)
10. Explain how muscular contractions move body parts and help maintain posture. (pp. 198–200)

**8.5 Smooth Muscle**

11. Distinguish between the structures and functions of multiunit smooth muscle and visceral smooth muscle. (p. 201)
12. Compare the contraction mechanisms of skeletal and smooth muscle fibers. (p. 201)

Anatomy & Physiology REVEALED aprevealed.com **Module 6:** Muscular System

### 8.6 Cardiac Muscle

**13.** Compare the contraction mechanisms of cardiac and skeletal muscle fibers. (pp. 201–202)

### 8.7 Skeletal Muscle Actions

**14.** Explain how the attachments, locations, and interactions of skeletal muscles make different movements possible. (pp. 202–204)

### 8.8 Major Skeletal Muscles

**15.** Identify and locate the major skeletal muscles of each body region. (pp. 204–217)

**16.** Identify the actions of the major skeletal muscles of each body region. (pp. 204–217)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**calat-** [something inserted] inter*calat*ed disc: Dense band that connects cardiac muscle cells.

**erg-** [work] syn*erg*ist: Muscle that works with an agonist to produce a movement.

**hyper-** [over, more] muscular *hyper*trophy: Enlargement of muscle fibers.

**inter-** [between] *inter*calated disc: Dense band that connects cardiac muscle cells.

**laten-** [hidden] *laten*t period: Time between application of a stimulus and the beginning of a muscle contraction.

**myo-** [muscle] *myo*fibril: Contractile structure within a muscle cell.

**sarco-** [flesh] *sarco*plasm: Material (cytoplasm) within a muscle fiber.

**syn-** [together] *syn*ergist: Muscle that works with an agonist to produce a movement.

**tetan-** [stiff] *tetan*ic contraction: Sustained muscular contraction.

**-troph** [well fed] muscular hyper*trophy*: Enlargement of muscle fibers.

---

## 8.1 | Introduction

Talking and walking, breathing and sneezing—in fact, all movements—require muscles. Muscles are organs composed of specialized cells that use chemical energy, obtained from nutrients, to pull on structures to which they are attached. Muscular actions also provide muscle tone, propel body fluids and food, generate the heartbeat, and distribute heat.

Muscle is of three types—skeletal muscle, smooth muscle, and cardiac muscle, as described in chapter 5 (p. 121). This chapter focuses mostly on skeletal muscle, which attaches to bones and is under conscious control. Smooth muscle and cardiac muscle are discussed briefly.

## 8.2 | Structure of a Skeletal Muscle

A skeletal muscle is an organ of the muscular system. It is composed of skeletal muscle tissue, nervous tissue, blood, and other connective tissues.

### Connective Tissue Coverings

Layers of dense connective tissue called **fascia** (fash′e-ah) separate an individual skeletal muscle from adjacent muscles and hold it in position (fig. 8.1). This connective tissue surrounds each muscle and may project beyond its end to form a cordlike tendon. Fibers in a tendon may intertwine with those in a bone's periosteum, attaching the muscle to the bone. In other cases, the connective tissue forms broad fibrous sheets called **aponeuroses** (ap″o-nu-ro′sez), which may attach to bone or to the coverings of adjacent muscles (see fig. 8.17*a*).

Fascia blends with the *epimysium*, a layer of connective tissue that closely surrounds each skeletal muscle (fig. 8.1). Other layers of connective tissue, called *perimysium,* extend inward from the epimysium and separate the muscle tissue into small sections. These

### CAREER CORNER
### Physical Therapy Assistant

The forty-eight-year-old man joined an over-thirty basketball league, and now he is paying for it. He lies on the gym floor, in pain, thanks to an overambitious jump shot. He had felt a sudden twinge in his knee, and now it is red and swelling.

In the emergency department of the nearest hospital, an orthopedist sends the man for an MRI scan, which reveals a small tear in the anterior cruciate ligament (ACL). The patient is willing to give up basketball and doesn't want surgery, so he sees a physical therapist twice a week for a month. A physical therapy assistant actually works with the man, leading him through a series of exercises that will restore full mobility.

The therapy, under the supervision of the physical therapist, begins with deep knee bends and progresses to lifting weights, stepping, squats, and using a single-leg bicycle that isolates and builds up the injured leg. The PT assistant gives her patient exercises to do daily, at home. The therapy builds the muscles around the knee to compensate for the hurt ACL, restoring full range of motion.

A physical therapy assistant must complete a two-year college program and pass a certification exam. PT assistants work in hospitals, skilled nursing facilities, private homes, schools, fitness centers, and workplaces.

sections contain bundles of skeletal muscle fibers called *fascicles* (fasciculi). Each muscle fiber within a fascicle (fasciculus) lies within a layer of connective tissue in the form of a thin covering called *endomysium*. Layers of connective tissue, therefore, enclose and separate all parts of a skeletal muscle. This organization allows the parts to move somewhat independently. Many blood vessels and nerves pass through these layers.

In *tendinitis*, a tendon (the attachment of a muscle to a bone) becomes painfully inflamed and swollen following injury or the repeated stress of athletic activity. If rest, physical therapy, and anti-inflammatory drugs do not alleviate tendinitis, then ultrasound can be applied to break up scar tissue. In *tenosynovitis*, the connective tissue sheath of the tendon (the tenosynovium) is inflamed. The tendons most commonly affected are those associated with the joint capsules of the shoulder, elbow, and hip and those that move the hand, thigh, and foot.

## Skeletal Muscle Fibers

A skeletal muscle fiber is a single cell that contracts (shortens) in response to stimulation and then relaxes when the stimulation ends. Each skeletal muscle fiber is a thin, elongated cylinder with rounded ends, and it may extend the full length of the muscle. Just beneath its cell membrane (or *sarcolemma*), the cytoplasm (or *sarcoplasm*) of the fiber has many small, oval nuclei and mitochondria (fig. 8.1). The sarcoplasm also contains many threadlike **myofibrils** (mi″o-fi′brilz) that lie parallel to one another.

Myofibrils play a fundamental role in muscle contraction. They consist of two kinds of protein filaments (myofilaments)—thick filaments composed of the protein **myosin** (mi′o-sin) and thin filaments mainly composed of the protein **actin** (ak′tin) (figs. 8.2 and 8.3). (Two other thin filament proteins, troponin and tropomyosin, are discussed later on page 193.) The organization of these filaments produces the characteristic alternating light and dark *striations*, or bands, of a skeletal muscle fiber.

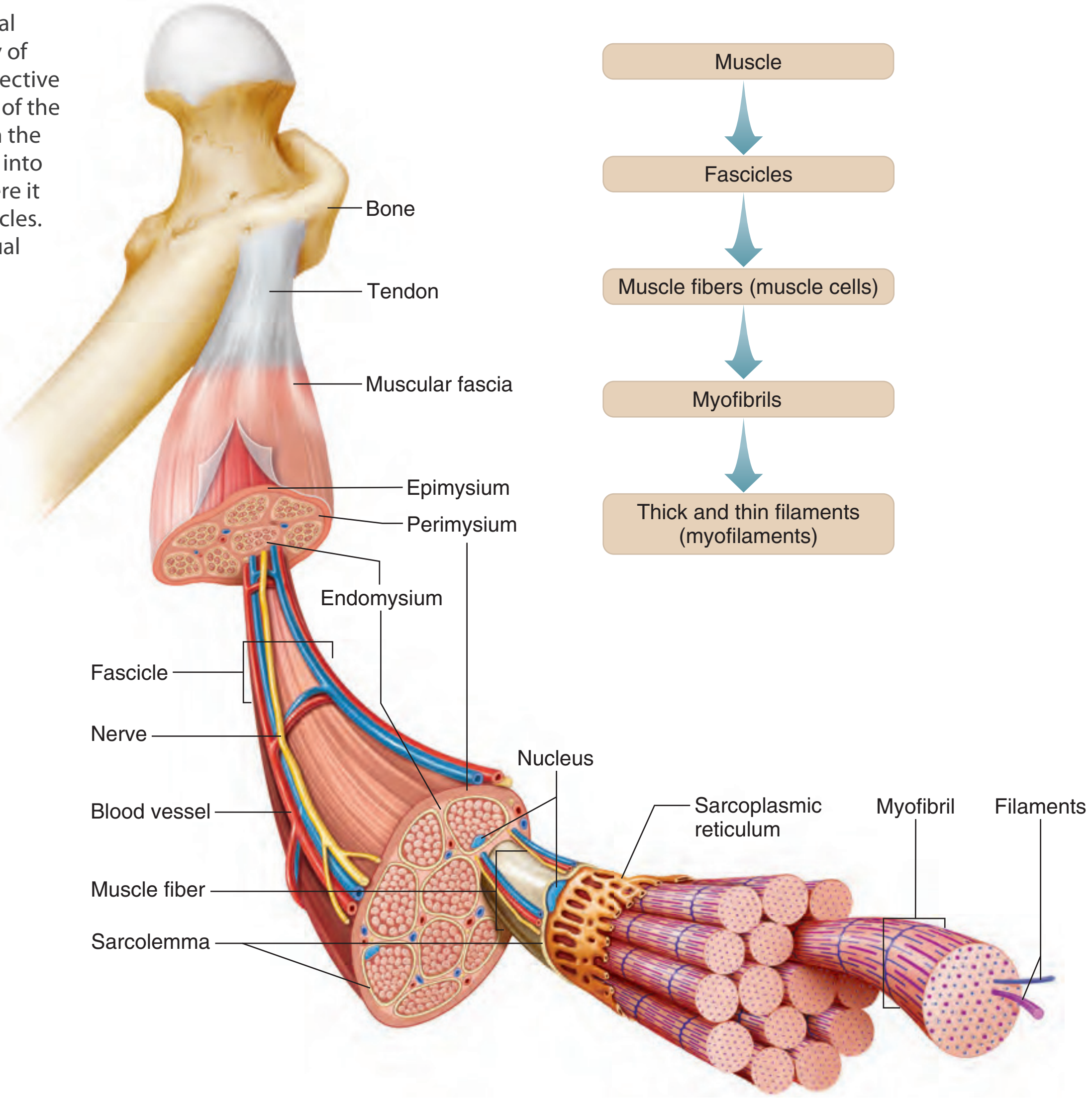
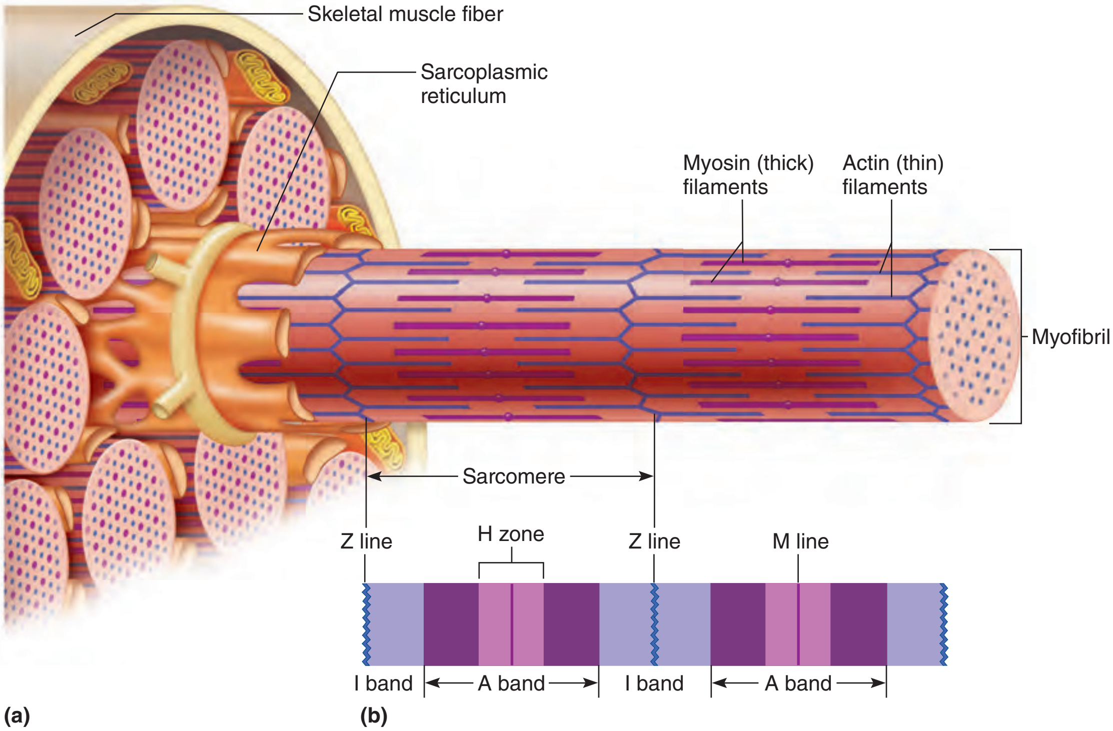

Bone
Tendon
Muscular fascia
Epimysium
Perimysium
Endomysium
Fascicle
Nerve
Blood vessel
Muscle fiber
Sarcolemma
Nucleus
Sarcoplasmic reticulum
Myofibril
Filaments
Muscle
Fascicles
Muscle fibers (muscle cells)
Myofibrils
Thick and thin filaments (myofilaments)

**FIGURE 8.1** APR A skeletal muscle is composed of a variety of tissues, including layers of connective tissue. Fascia covers the surface of the muscle, epimysium lies beneath the fascia, and perimysium extends into the structure of the muscle where it separates muscle cells into fascicles. Endomysium separates individual muscle fibers.

**FIGURE 8.2** APR Skeletal muscle fiber. **(a)** A skeletal muscle fiber contains many myofibrils, each consisting of **(b)** repeating units called sarcomeres. The characteristic striations of a sarcomere reflect the organization of actin and myosin filaments.


Skeletal muscle fiber
Sarcoplasmic reticulum
Myosin (thick) filaments
Actin (thin) filaments
Myofibril
Sarcomere
Z line
H zone
Z line
M line
I band
A band
I band
A band
(a)
(b)

The striations of skeletal muscle form a repeating pattern of units called **sarcomeres** (sar′ko-mĕrz) along each muscle fiber. The myofibrils may be thought of as sarcomeres joined end-to-end (fig. 8.2). Muscle fibers, and in a way muscles themselves, may be thought of as a collection of sarcomeres. Sarcomeres are discussed later as the functional units of muscle contraction (p. 193).

The striation pattern of skeletal muscle fibers has two main parts. The first, the *I bands* (the light bands), are composed of thin actin filaments directly attached to structures called *Z lines*. The second part of the striation pattern consists of the *A bands* (the dark bands), which are composed of thick myosin filaments overlapping thin actin filaments. The A band consists of a region where the thick and thin filaments overlap, and a central region (*H zone*) consisting only of thick filaments, plus a thickening known as the *M line* (fig. 8.2). The M line consists of proteins that help hold the thick filaments in place. A sarcomere extends from one Z line to the next (figs. 8.2 and 8.3).

Within the sarcoplasm of a muscle fiber is a network of membranous channels that surrounds each myofibril and runs parallel to it (fig. 8.4). These membranes form the **sarcoplasmic reticulum,** which corresponds to the endoplasmic reticulum of other cells. Another set of membranous channels, called **transverse tubules** (T tubules), extends inward as invaginations from the fiber's membrane and passes

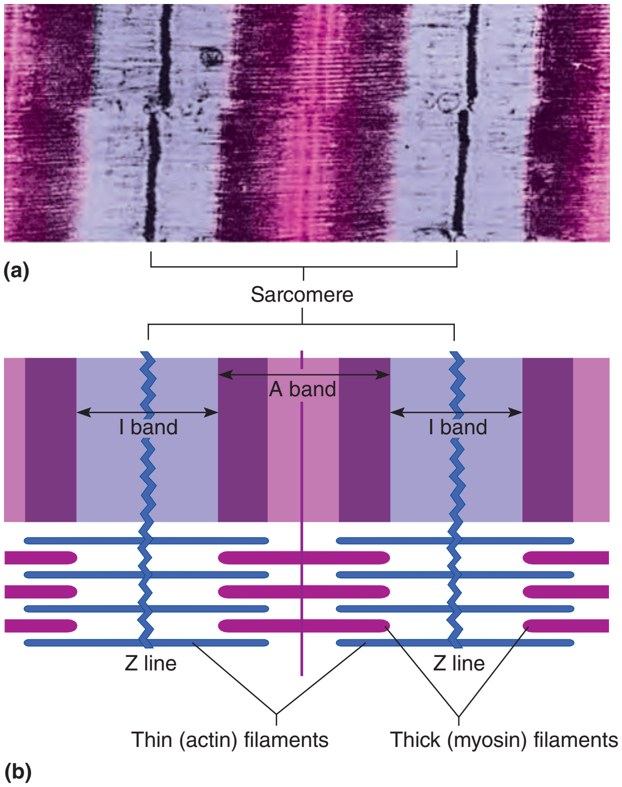

(a)
Sarcomere
A band
I band
I band
Z line
Z line
Thin (actin) filaments
Thick (myosin) filaments
(b)

**FIGURE 8.3** APR A sarcomere is a functional unit of muscle contraction. **(a)** Micrograph (16,000×). **(b)** The spatial relationship of thin and thick filaments in a sarcomere makes contraction possible.

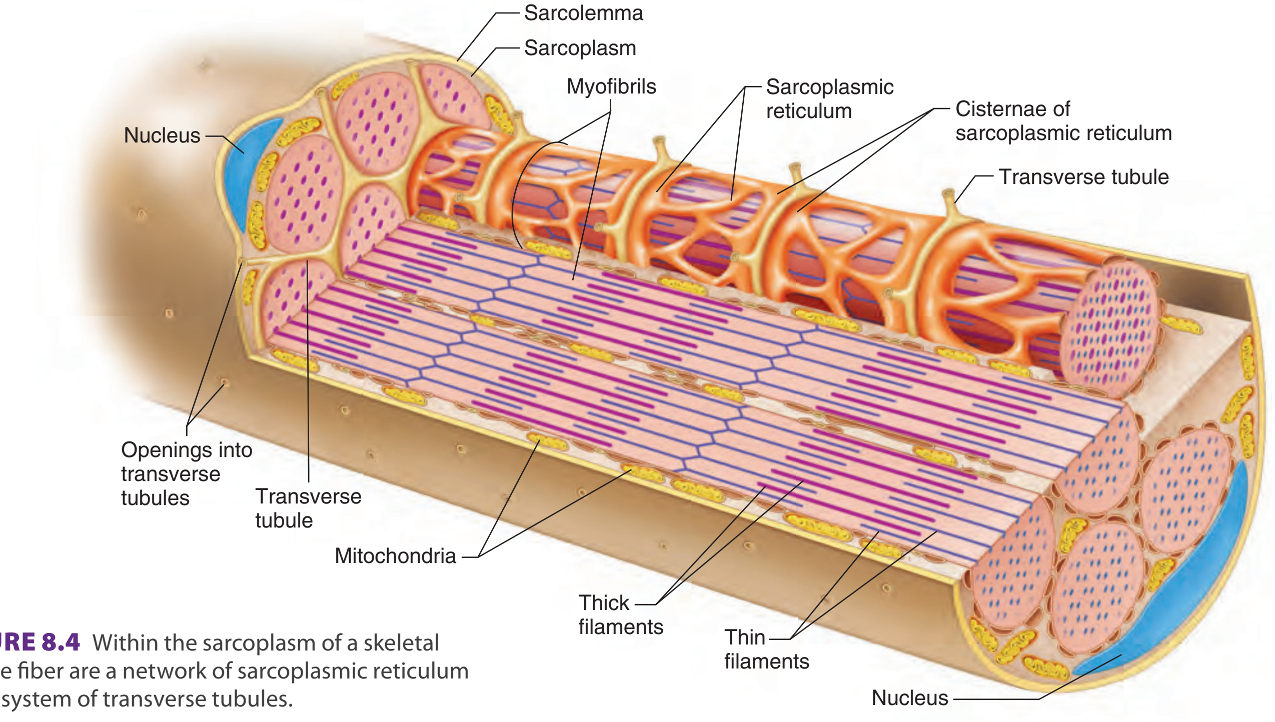


**FIGURE 8.4** Within the sarcoplasm of a skeletal muscle fiber are a network of sarcoplasmic reticulum and a system of transverse tubules.

all the way through the fiber. Thus, each transverse tubule opens to the outside of the muscle fiber and contains extracellular fluid. Furthermore, each transverse tubule lies between two enlarged portions of the sarcoplasmic reticulum called *cisternae,* near the region where the actin and myosin filaments overlap. The sarcoplasmic reticulum and transverse tubules activate the muscle contraction mechanism when the muscle fiber is stimulated.

Muscle fibers and their associated connective tissues are flexible but can tear if overstretched. This type of injury, common in athletes, is called *muscle strain*. The severity of the injury depends on the degree of damage the tissues sustain. If the strain is mild, only a few muscle fibers are injured, the fascia remains intact, and loss of function is minimal. In a severe strain, however, many muscle fibers as well as the fascia tear, and muscle function may be completely lost. Such a severe strain is painful and produces discoloration and swelling.

## PRACTICE

1. Describe how connective tissue is part of a skeletal muscle.
2. Describe the general structure of a skeletal muscle fiber.
3. Explain why skeletal muscle fibers appear striated.
4. Explain the relationship between the sarcoplasmic reticulum and the transverse tubules.

## Neuromuscular Junction

Recall from chapter 5 (p. 122) that neurons (nerve cells) play a role in body communication by conducting electrical impulses. Neurons that control effectors are called **motor neurons.** Normally a skeletal muscle fiber contracts only when stimulated by a motor neuron. The opening vignette to chapter 3 (p. 60) describes amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease), which affects motor neurons that control skeletal muscles.

Each skeletal muscle fiber is functionally (but not physically) connected to the axon of a motor neuron that passes outward from the brain or the spinal cord, in much the same way that you can talk into a cell phone although your mouth is not in direct physical contact with it. This functional connection is called a **synapse** (sin′aps). Neurons communicate with the cells that they control by releasing chemicals, called **neurotransmitters** (nu″ro-trans′mit-erz), at synapses.

The synapse between the motor neuron and the muscle fiber that it controls is called a **neuromuscular junction.** Here, the muscle fiber membrane is specialized to form a **motor end plate.** In this region of the muscle fiber, nuclei and mitochondria are abundant, and the cell membrane (sarcolemma) is extensively folded. A small gap called the **synaptic cleft** separates the membrane of the neuron and the membrane of the muscle fiber (fig. 8.5).

The end of the motor neuron extends fine projections into recesses of the muscle fiber. The cytoplasm at the distal ends of these motor neuron axons is rich in mitochondria and contains many tiny vesicles (synaptic vesicles) that store neurotransmitter.

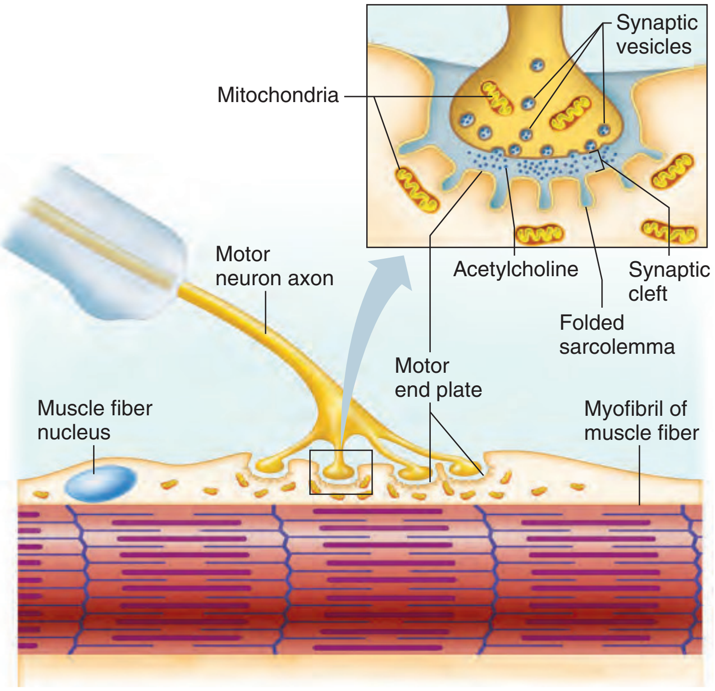


**FIGURE 8.5** APR A neuromuscular junction includes the end of a motor neuron and the motor end plate of a muscle fiber.

**Q** *How does neurotransmitter released into the synaptic cleft reach the muscle fiber membrane?*

**Answer can be found in Appendix F on page 582.**

### PRACTICE

5. Which two structures approach each other at a neuromuscular junction?
6. Describe a motor end plate.
7. What is the function of a neurotransmitter?

## 8.3 | Skeletal Muscle Contraction

A muscle fiber contraction involves an interaction of organelles and molecules in which myosin binds to actin and exerts a pulling force. The result is a movement within the myofibrils in which the filaments of actin and myosin slide past one another, increasing the area of overlap. This action shortens the muscle fiber, which then pulls on its attachments.

### Role of Myosin and Actin

A myosin molecule is composed of two twisted protein strands with globular parts called heads projecting outward along their lengths. Many of these molecules together compose a myosin (thick) filament (fig. 8.6). An actin molecule is a globular structure with a binding site to which the myosin heads can attach. Many actin molecules twist into a double strand (helix), forming an actin (thin) filament. The proteins **troponin** and **tropomyosin** are also part of the actin filament (fig. 8.6).

The sarcomere is considered the functional unit of skeletal muscles because we can describe the contraction of an entire skeletal muscle in terms of the shortening of the sarcomeres within its muscle fibers. The force that shortens the sarcomeres comes from the myosin heads pulling on the thin filaments. A myosin head can attach to an actin binding site, forming a *cross-bridge*, and bend slightly, pulling on the actin filament. Then the myosin head can release, straighten, combine with another binding site further down the actin filament, and pull again (fig. 8.7).

The **sliding filament model** of muscle contraction includes all of these actin-myosin interactions and is named for how the sarcomeres shorten. Thick and thin filaments do not change length. Rather, they slide past one another, with the thin filaments moving toward the center of the sarcomere from both ends (fig. 8.8).

The myosin heads contain an enzyme, **ATPase,** which catalyzes the breakdown of ATP to ADP and phosphate (see chapter 4, p. 91). This reaction provides energy that puts the myosin head in a "cocked" position. When a cocked myosin head binds to the actin, forming a cross-bridge, it pulls on the thin filament. After the cross-bridge pulls, another ATP binding to the myosin breaks the cross-bridge, releasing the myosin head from the actin even before the ATP splits. The ATPase then catalyzes the breakdown of ATP to ADP and phosphate, putting the myosin head in a "cocked" position again. This cycle repeats as long as ATP is available as an energy source and as long as the muscle fiber is stimulated to contract.

### Stimulus for Contraction APR

A skeletal muscle fiber normally does not contract until a neurotransmitter stimulates it. The neurotransmitter in skeletal muscle contraction is **acetylcholine** (as″ĕ-til-ko′lēn).

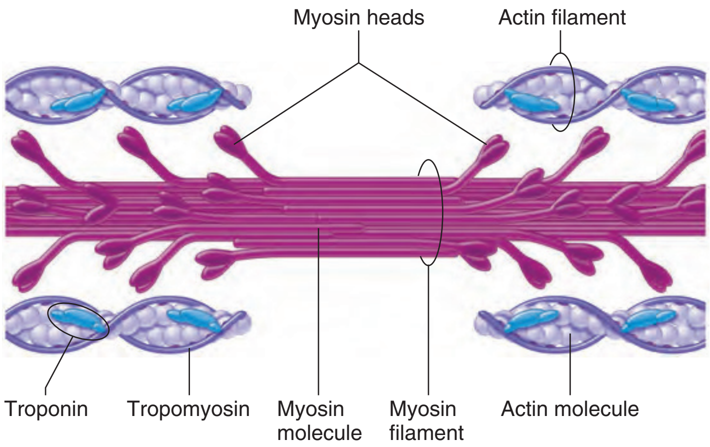


**FIGURE 8.6** Thick filaments are composed of the protein myosin, and thin filaments are composed primarily of the protein actin. Myosin molecules have globular heads that extend toward nearby actin filaments.

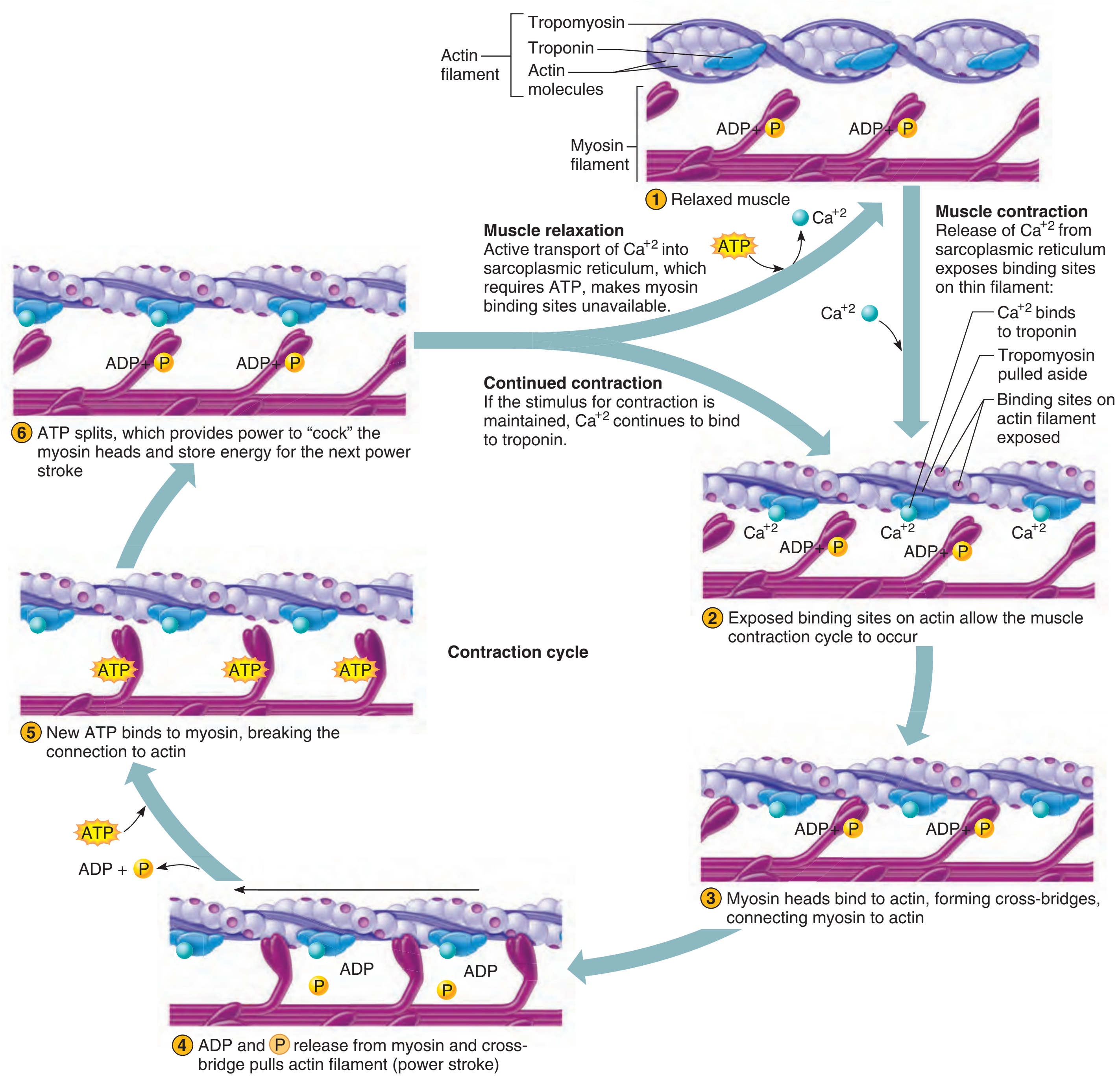

Actin filament
Tropomyosin
Troponin
Actin molecules
Myosin filament
ADP + P
ADP + P
① Relaxed muscle
Muscle relaxation
Active transport of Ca+2 into sarcoplasmic reticulum, which requires ATP, makes myosin binding sites unavailable.
ATP
Ca+2
Muscle contraction
Release of Ca+2 from sarcoplasmic reticulum exposes binding sites on thin filament:
Ca+2
Ca+2 binds to troponin
Tropomyosin pulled aside
Binding sites on actin filament exposed
ADP + P
ADP + P
⑥ ATP splits, which provides power to "cock" the myosin heads and store energy for the next power stroke
Continued contraction
If the stimulus for contraction is maintained, Ca+2 continues to bind to troponin.
Ca+2
ADP + P
Ca+2
ADP + P
Ca+2
② Exposed binding sites on actin allow the muscle contraction cycle to occur
Contraction cycle
ATP
ATP
ATP
⑤ New ATP binds to myosin, breaking the connection to actin
ADP + P
ADP + P
③ Myosin heads bind to actin, forming cross-bridges, connecting myosin to actin
ATP
ADP + P
ADP
P
ADP
P
④ ADP and P release from myosin and cross-bridge pulls actin filament (power stroke)

**FIGURE 8.7** The sliding filament model. **(1)** Relaxed muscle. **(2)** and **(3)** When calcium ion concentration rises, binding sites on actin filaments open, and myosin heads bind to the actin forming cross-bridges. **(4)** Upon binding to actin, myosin heads spring from the cocked position and pull on actin filaments. **(5)** ATP binds (but is not yet broken down), causing the myosin heads to release from the actin filament. **(6)** ATP breakdown provides energy to "cock" the unattached myosin heads. As long as ATP and calcium ions are present, the cycle continues. When the calcium ion concentration is low, the muscle is relaxed.

This neurotransmitter is synthesized in the cytoplasm of the motor neuron and stored in vesicles at the distal end of the motor neuron axons. When an impulse (described in chapter 9, p. 236) reaches the end of a motor neuron axon, some of the vesicles release their acetylcholine into the synaptic cleft, the space between the motor neuron axon terminal and the motor end plate (see fig. 8.5).

Acetylcholine diffuses rapidly across the synaptic cleft and binds to specific protein molecules (receptors) in the muscle fiber membrane, increasing membrane permeability to sodium ions. Entry of these charged particles into the muscle cell stimulates an electrical impulse much like the impulse on the motor neuron. The impulse passes in all directions over the surface of the muscle fiber membrane and travels through the

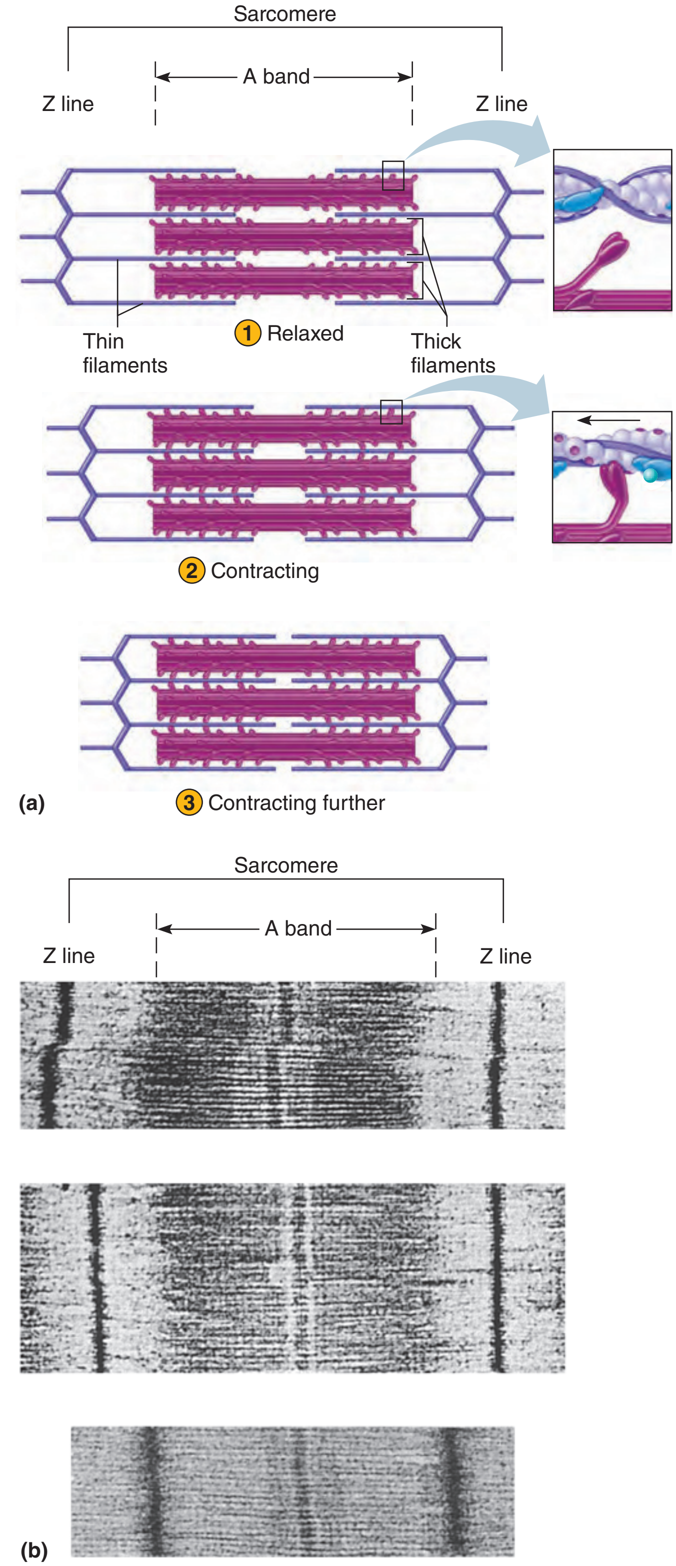


**FIGURE 8.8** APR When a skeletal muscle contracts, **(a)** individual sarcomeres shorten as thin filaments slide past thick filaments toward the center of the sarcomere. **(b)** This transmission electron micrograph shows a sarcomere shortening during muscle contraction (23,000×).

*What happens to the length of the thick and thin filaments during contraction?*

**Answer can be found in Appendix F on page 582.**

transverse tubules, deep into the fiber, until it reaches the sarcoplasmic reticulum (see fig. 8.4).

The sarcoplasmic reticulum contains a high concentration of calcium ions. In response to a muscle impulse, the membranes of the cisternae become more permeable to these ions, and the calcium ions diffuse into the sarcoplasm of the muscle fiber.

When a high concentration of calcium ions is in the sarcoplasm, troponin and tropomyosin interact in a way that exposes binding sites on actin. As a result, cross-bridge linkages form between the actin and myosin filaments, and the muscle fiber contracts (see figs. 8.7 and 8.8). The contraction, which also requires ATP, continues as long as the motor neuron releases acetylcholine.

When nervous stimulation ceases, two events lead to muscle relaxation. First, the acetylcholine that stimulated the muscle fiber is rapidly decomposed by the enzyme **acetylcholinesterase** (as′ĕ-til-ko″lin-es′ter-ās). This enzyme is present at the neuromuscular junction on the membranes of the motor end plate. Acetylcholinesterase prevents a single impulse on a motor neuron from continuously stimulating the muscle fiber.

The second event in muscle relaxation takes place once acetylcholine is broken down and the stimulus to the muscle fiber ceases. Calcium ions are actively transported back into the sarcoplasmic reticulum, which decreases the calcium ion concentration of the sarcoplasm. The cross-bridge linkages between actin and myosin filaments break, and consequently, the muscle fiber relaxes. Table 8.1 summarizes the major events leading to muscle contraction and relaxation.

## PRACTICE

8. Explain how an impulse on a motor neuron can trigger a muscle contraction.
9. Explain how the filaments of a myofibril interact during muscle contraction.

## Energy Sources for Contraction

ATP molecules supply the energy for muscle fiber contraction. However, a muscle fiber has only enough ATP to enable it to contract for a very short time. Therefore, when a fiber is active, ATP must be regenerated.

The initial source of energy available to a contracting muscle comes from existing ATP molecules in the cell. Almost immediately, however, cells must regenerate ATP from ADP and phosphate. The molecule that initially makes this possible is **creatine phosphate** (kre′ah-tin fos′fāt). Like ATP, creatine phosphate contains high-energy phosphate bonds. When ATP supply is sufficient, an enzyme in the mitochondria (creatine phosphokinase) catalyzes the synthesis of creatine phosphate, which stores excess energy in its phosphate bonds (fig. 8.9).

## TABLE 8.1 Major Events of Muscle Contraction and Relaxation

**Muscle Fiber Contraction**

1. An impulse travels down a motor neuron axon.
2. The motor neuron terminal releases the neurotransmitter acetylcholine (ACh).
3. ACh binds to ACh receptors on the muscle fiber membrane.
4. The sarcolemma is stimulated. An impulse travels over the surface of the muscle fiber and deep into the fiber through the transverse tubules.
5. The impulse reaches the sarcoplasmic reticulum, and calcium channels open.
6. Calcium ions diffuse from the sarcoplasmic reticulum into the sarcoplasm and bind to troponin molecules.
7. Tropomyosin molecules move and expose specific sites on actin where myosin heads can bind.
8. Actin and myosin link, forming cross-bridges.
9. Thin (actin) filaments are pulled toward the center of the sarcomere by pulling of the cross-bridges.
10. The muscle fiber shortens as a contraction occurs.

**Muscle Fiber Relaxation**

1. Acetylcholinesterase decomposes acetylcholine, and the muscle fiber membrane is no longer stimulated.
2. Calcium ions are actively transported into the sarcoplasmic reticulum.
3. ATP breaks cross-bridge linkages between actin and myosin filaments without breakdown of the ATP itself.
4. Breakdown of ATP "cocks" the myosin heads.
5. Troponin and tropomyosin molecules block the interaction between myosin and actin filaments.
6. The muscle fiber remains relaxed, yet ready, until stimulated again.

Creatine phosphate is four to six times more abundant in muscle fibers than ATP, but it cannot directly supply energy to a cell's energy-utilizing reactions. Instead, as ATP decomposes, the energy from creatine phosphate can be transferred to ADP molecules, converting them back into ATP. Active muscle, however, rapidly exhausts the supply of creatine phosphate. When this happens, the muscle fibers use cellular respiration of glucose as an energy source for synthesizing ATP.

## Oxygen Supply and Cellular Respiration

Glycolysis can take place in the absence of oxygen, as discussed in chapter 4 (p. 91). However, the more complete breakdown of glucose occurs in the mitochondria and requires oxygen. The blood carries the oxygen from the lungs to body cells to support this aerobic respiration. Red blood cells carry the oxygen, loosely bound to molecules of **hemoglobin,** the pigment responsible for the red color of blood.

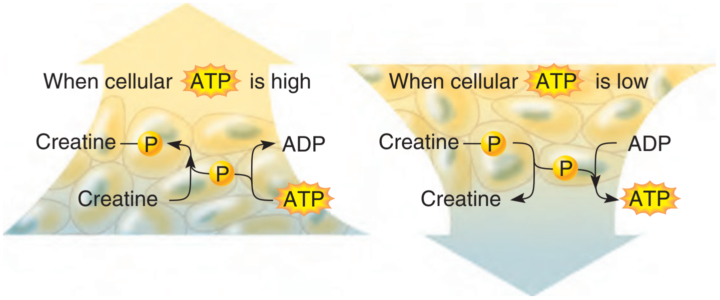


**FIGURE 8.9** Creatine phosphate may be used to replenish ATP stores when ATP levels in a muscle cell are low.

Another pigment, **myoglobin,** is synthesized in muscle cells and imparts the reddish-brown color of skeletal muscle tissue. Like hemoglobin, myoglobin can combine loosely with oxygen. Myoglobin's ability to temporarily store oxygen increases the amount of oxygen available in the muscle cells to support aerobic respiration (fig. 8.10).

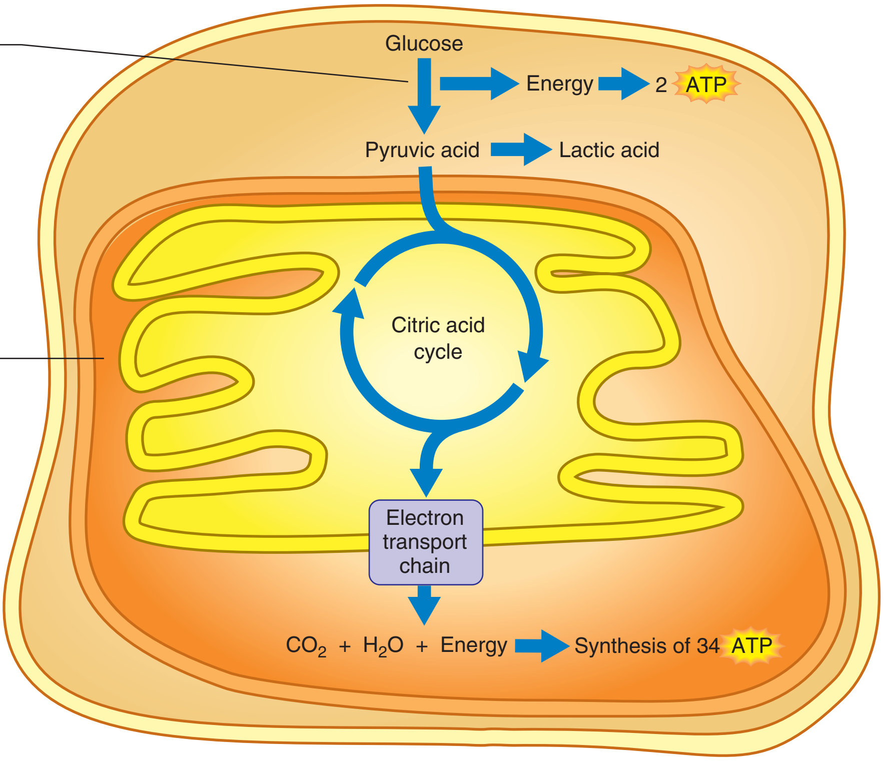
## Oxygen Debt

When a person is resting or is moderately active, the respiratory and cardiovascular systems can usually supply sufficient oxygen to skeletal muscles to support aerobic respiration. However, this may not be the case when skeletal muscles are used strenuously for even a minute or two. In this situation, muscle fibers increasingly rely on anaerobic respiration to obtain energy.

In anaerobic respiration, glucose molecules are broken down by glycolysis to yield *pyruvic acid* (see chapter 4, p. 91). Because the oxygen supply is low, however, the pyruvic acid reacts to produce *lactic acid* (fig. 8.10). Lactic acid dissociates rapidly to form lactate ion (lactate) and hydrogen ion, which may accumulate in the muscles. Lactate leaves muscle cells by facilitated diffusion, enters the bloodstream and eventually reaches the liver. In liver cells, reactions requiring ATP synthesize glucose from lactate.

During strenuous exercise, available oxygen is used primarily to synthesize the ATP the muscle fiber requires to contract, rather than to make ATP for synthesizing glucose from lactate. Consequently, as lactate accumulates, a person develops an **oxygen debt** (ok′sĭ-jen det) that must be repaid. Oxygen debt equals the amount of oxygen that liver cells require to convert the accumulated lactate into glucose, plus the amount muscle cells require to restore ATP and creatine phosphate to their original concentrations and to return blood and tissue oxygen levels to normal. The conversion of lactate back into glucose is slow. Repaying an oxygen debt following vigorous exercise may take several hours.

The metabolic capacity of a muscle may change with physical training. With high-intensity exercise,



① Oxygen carried from lungs by hemoglobin in red blood cells is temporarily stored in muscle cells by myoglobin, increasing the amount of oxygen available to support aerobic respiration.

② In the absence of sufficient oxygen, aerobic respiration cannot continue, and glycolysis leads to lactic acid formation.

**FIGURE 8.10** The oxygen required to support aerobic respiration is carried in the blood and stored in myoglobin. In the absence of sufficient oxygen, pyruvic acid reacts to produce lactic acid by anaerobic respiration. The maximum number of ATPs generated per glucose molecule varies with cell type; in skeletal muscle, it is 36 (2 + 34).

which depends more on glycolysis for ATP, a muscle synthesizes more glycolytic enzymes, and its capacity for glycolysis increases. With aerobic exercise, more capillaries and mitochondria form, and the muscle's capacity for aerobic respiration is greater. Table 8.2 summarizes muscle metabolism, and Clinical Application 8.1 discusses abuse of steroid drugs to enhance muscle performance.

## Muscle Fatigue

A muscle exercised strenuously for a prolonged period may lose its ability to contract, a condition called *fatigue*. The underlying causes of fatigue are not completely understood, but a number of factors may be involved, including electrolyte imbalances and decreased ATP levels in the muscle cells. For many years fatigue has been attributed to the increased lactic acid production associated with anaerobic respiration. If pH drops sufficiently, muscle fibers may no longer respond to stimulation. However, recent studies have raised some doubts about the role of lactic acid in fatigue, and research in this area is ongoing.

Occasionally a muscle becomes fatigued and cramps at the same time. A cramp is a painful condition in which a muscle undergoes a sustained involuntary contraction. Cramps are thought to occur when changes in the extracellular fluid surrounding the muscle fibers and their motor neurons somehow trigger uncontrolled stimulation of the muscle.

Several hours after death, skeletal muscles partially contract and become rigid, fixing the joints in place. This condition, *rigor mortis,* may continue for 72 hours or more. It results from an increase in membrane permeability to calcium ions and a decrease in ATP in muscle fibers, which prevents relaxation. The actin and myosin filaments of the muscle fibers remain linked until the muscles begin to decompose.

## Heat Production

Less than half of the energy released in cellular respiration is transferred to ATP, and the rest becomes heat. Although all active cells generate heat, muscle tissue is

**TABLE 8.2** **Muscle Metabolism**

| | | |
|---|---|---|
| *Type of Exercise* | Low to moderate intensity: Blood flow provides sufficient oxygen for cellular requirements | High intensity: Oxygen supply is not sufficient for cellular requirements |
| *Pathway Used* | Glycolysis, leading to pyruvic acid formation and aerobic respiration | Glycolysis, leading to lactic acid formation |
| *ATP Production* | 36 ATP per glucose for skeletal muscle | 2 ATP per glucose |
| *Waste Product* | Carbon dioxide is exhaled | Lactic acid accumulates |

## CLINICAL APPLICATION 8.1

## Steroids and Athletes—An Unhealthy Combination

It seems that not a year goes by without a few famous athletes confessing to, or being caught using, steroid hormones to bulk up their muscles to improve performance. High school and college athletes abuse steroids too. Athletes who abuse steroids seek the hormone's ability to increase muscular strength. They are caught when the steroids or their breakdown products are detected in urine or when natural testosterone levels plummet in a negative feedback response to the outside hormone supply (fig. 8A). But improved performance today may have consequences tomorrow. Steroids hasten adulthood, stunting height and causing early hair loss. In males, excess steroid hormones lead to breast development, and in females to a deepened voice, hairiness, and a male physique. The kidneys, liver, and heart may be damaged, and atherosclerosis may develop because steroids raise LDL cholesterol. In males, the body mistakes the synthetic steroids for the natural hormone and lowers its own production of testosterone. Infertility may result. Steroids can also cause psychiatric symptoms, including delusions, depression, and violence.

Anabolic steroids have been used for medical purposes since the 1930s, to treat underdevelopment of the testes and the resulting testosterone deficiency, anemia, and muscle-wasting disorders. Today, they are used to treat wasting associated with AIDS.

**FIGURE 8A** Sprinter Ben Johnson ran away with the gold medal in the 100-meter race at the 1988 Summer Olympics—but then had to return the award when traces of a steroid drug showed up in his urine. Drug abuse continues to be a problem among amateur as well as professional athletes.

a major heat source because muscle is such a large proportion of the total body mass. Blood transports heat generated in muscle to other tissues, which helps maintain body temperature.

**PRACTICE**

10. Which biochemicals provide the energy to regenerate ATP?
11. What are the sources of oxygen for aerobic respiration?
12. How are lactic acid, oxygen debt, and muscle fatigue related?
13. What is the relationship between cellular respiration and heat production?

## 8.4 | Muscular Responses

One way to observe muscle contraction is to remove a single muscle fiber from a skeletal muscle and connect it to a device that records changes in the fiber's length. Such experiments usually require an electrical device that can produce stimuli of varying strengths and frequencies.

### Threshold Stimulus

When an isolated muscle fiber is exposed to a series of stimuli of increasing strength, the fiber remains unresponsive until a certain strength of stimulation called the **threshold stimulus** (thresh′old stim′u-lus) is applied. Once threshold is reached, an electrical impulse is generated that spreads throughout the muscle fiber, releasing enough calcium ions from the sarcoplasmic reticulum to activate cross-bridge binding and contract that fiber. A single impulse in a motor neuron normally releases enough ACh to bring the muscle fibers in its motor unit to threshold, generating an impulse in each muscle fiber.

### Recording of a Muscle Contraction

The contractile response of a single muscle fiber to a single impulse is called a **twitch.** A twitch consists of a period of contraction, during which the fiber pulls at its attachments, followed by a period of relaxation, during which the pulling force declines. These events can be recorded in a pattern called a myogram (fig. 8.11). Note that a twitch has a brief delay between the time of stimulation and the beginning of contraction. This is the **latent period,** which in human muscle may be less than 2 milliseconds.

A muscle fiber brought to threshold under a given set of conditions tends to contract completely, such that each twitch generates the same force. This phenomenon is termed an *all-or-none* response. The description, though, is misleading, because in normal use of muscles, the force generated by muscle fibers and by whole muscles must vary.

Understanding how individual muscle fibers contract is important for understanding how muscles work, but such contractions by themselves are of little significance in day-to-day activities. Rather, the actions we need to perform usually require the contraction of multiple muscle fibers simultaneously. To record how a whole muscle responds to stimulation, a skeletal muscle can be removed from a small animal, such as a frog, and mounted on a special device. The muscle is then stimulated electrically, and when it contracts, it pulls on a lever. The lever's movement is recorded as a myogram. Because the myogram results from the combined twitches of muscle fibers taking part in the contraction, it looks like the twitch contraction depicted in figure 8.11.

Muscle fibers vary in contraction speed. Clinical Application 8.2 describes two types of fibers—the fatigue-resistant slow twitch and the fatigable fast twitch. Muscle fibers are either slow twitch or fast twitch.

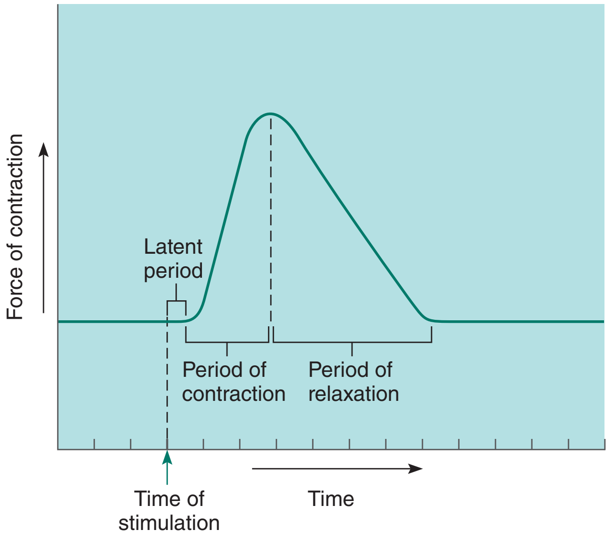


**FIGURE 8.11** A myogram of a single muscle twitch.

The skeletal muscles of an average person have about half fast-twitch and half slow-twitch muscle fibers. In contrast, the muscles of an Olympic sprinter typically have more than 80% fast-twitch muscle fibers, and those of an Olympic marathoner, more than 90% slow-twitch muscle fibers.

Contractions of whole muscles enable us to perform everyday activities, but the force generated by those contractions must be controlled. For example, holding a styrofoam cup of coffee firmly enough that it does not slip through our fingers, but not so forcefully as to crush it, requires precise control of contractile force. In the whole muscle, the degree of tension developed reflects (1) the frequency at which individual muscle fibers are stimulated and (2) how many fibers take part in the overall contraction of the muscle.

## Summation

The force that a muscle fiber can generate is not limited to the maximum force of a single twitch. A muscle fiber exposed to a series of stimuli of increasing frequency reaches a point when it is unable to completely relax before the next stimulus in the series arrives. When this happens, the force of individual twitches combines by the process of **summation.** At higher frequencies of stimulation, as the time spent in relaxation becomes very brief, a condition called partial tetany results. If the frequency of contraction is so rapid that the contraction lacks even partial relaxation, it is called a **complete tetanic** (tĕ-tan′ik) **contraction,** or tetanus (fig. 8.12).

## Recruitment of Motor Units

While summation increases the force of contraction of a single muscle fiber, a whole muscle can generate more force if more muscle fibers are involved in the contraction. A muscle fiber typically has a single motor end plate. The axons of motor neurons, however, are densely branched, which enables one such axon to connect to many muscle fibers. Together, a motor neuron and the muscle fibers that it controls constitute a **motor unit** (mo′tor u′nit) (fig. 8.13). Each motor unit is a functional unit because an impulse in its motor neuron will cause all of the muscle fibers in that motor unit to contract at the same time. A whole muscle is composed of many motor units controlled by different motor neurons. Like muscle fibers, motor neurons must be brought to threshold before an impulse is generated. It turns out that some motor neurons are more easily brought to threshold than others. If only the more sensitive motor neurons reach threshold, few motor units contract. At higher intensities of stimulation, other motor neurons are brought to threshold, and more motor units are activated. An increase in the number of motor units being activated during a contraction is called **recruitment** (re-kroot′ment). As the intensity of stimulation increases,

CLINICAL APPLICATION 8.2

## Use and Disuse of Skeletal Muscles

Skeletal muscles are very responsive to use and disuse. Forcefully exercised muscles enlarge, which is called *muscular hypertrophy.* Conversely, an unused muscle undergoes *atrophy,* decreasing in size and strength.

The way a muscle responds to use also depends on the type of exercise. A muscle contracting with lower intensity, during swimming or running, activates *slow-twitch fibers,* which are oxidative and thus fatigue-resistant. With use, these specialized muscle fibers develop more mitochondria, and more extensive capillary networks envelop them. Such changes increase the slow-twitch fibers' ability to resist fatigue during prolonged exercise, although their sizes and strengths may remain unchanged.

Forceful exercise, such as weightlifting, in which a muscle exerts more than 75% of its maximum tension, utilizes *fast-twitch fibers,* which may be glycolytic and thus fatigable. In response to strenuous exercise, these fibers produce new filaments of actin and myosin, the diameters of the muscle fibers increase, and the entire muscle enlarges. However, the muscular hypertrophy is not caused by the formation of new muscle fibers.

The strength of a muscular contraction is directly proportional to the diameter of the activated muscle fibers. Consequently, an enlarged muscle can produce stronger contractions than before. Such a change, however, does not increase the muscle's ability to resist fatigue during activities like swimming or running.

If regular exercise stops, the capillary networks shrink, and the number of mitochondria within the muscle fibers drops. The number of actin and myosin filaments decreases, and the entire muscle atrophies. Such atrophy commonly occurs when accidents or diseases block motor nerve impulses from reaching muscle fibers. An unused muscle may shrink to less than half its usual size within a few weeks .

The fibers of muscles whose motor neurons are severed not only shrink, but also may fragment and, in time, be replaced by fat or fibrous connective tissue. However, reinnervation within the first few months following an injury may restore muscle function.

Astronauts experience muscle atrophy and impaired performance with long-term exposure to the microgravity environment of space. Customized workouts using special resistance equipment can minimize the changes in muscle structure and function. Otherwise, loss of muscle mass can make a thirty-year-old's muscles work like those of an eighty-year-old.

recruitment of motor units continues until, finally, all motor units in that muscle are activated and the muscle contracts with maximal tension.

## Sustained Contractions

Summation and recruitment together can produce a *sustained contraction* of increasing strength. Sustained contractions of whole muscles enable us to perform everyday activities. Such contractions are responses to a rapid series of impulses transmitted from the brain and spinal cord on motor neuron axons.

Even when a muscle appears to be at rest, its fibers undergo some sustained contraction. This is called **muscle tone** (tonus). Muscle tone is a response to nervous stimulation that originates repeatedly from the spinal cord and stimulates only a few muscle fibers at a time. Muscle tone is particularly important in maintaining posture. If muscle tone is suddenly lost, as happens when a person loses consciousness, the body collapses.

When skeletal muscles contract very forcefully, they may generate up to fifty pounds of pull for each square inch of muscle cross section. Large muscles, such as those in the thigh, can pull with several hundred pounds of force. This force may be so great that the tendons of muscles tear away from their attachments to the bones (*muscle pull*).

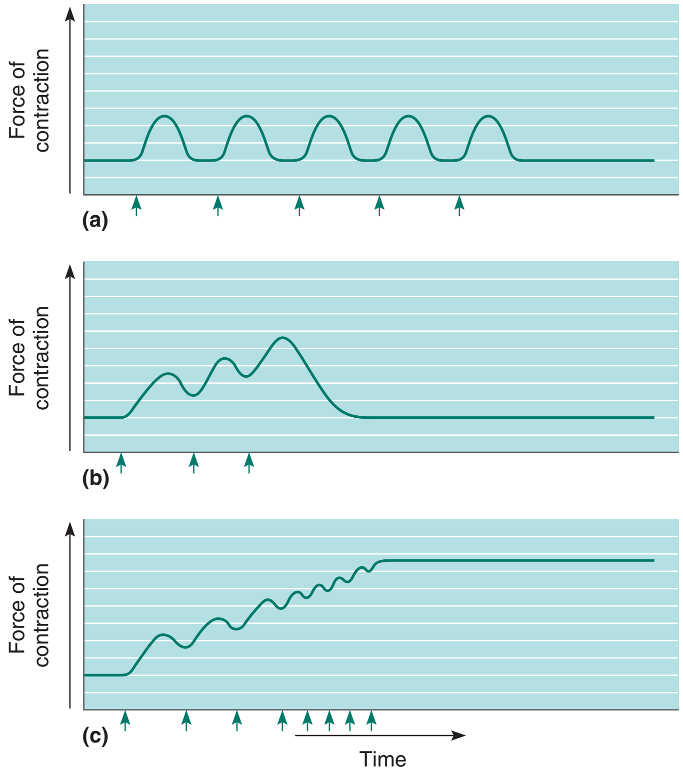


**FIGURE 8.12** Myograms of **(a)** a series of twitches, **(b)** summation, and **(c)** a tetanic contraction. Note that stimulation frequency increases from one myogram to the next.

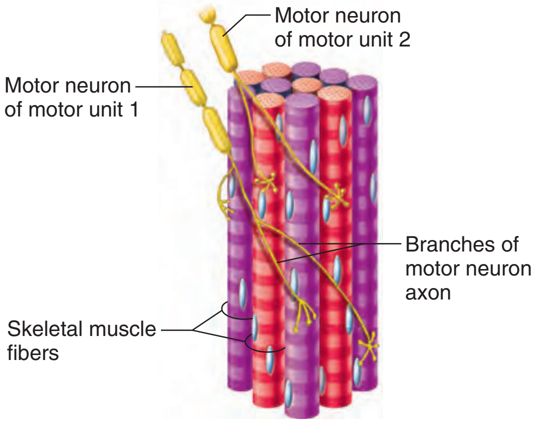

Motor neuron of motor unit 2
Motor neuron of motor unit 1
Branches of motor neuron axon
Skeletal muscle fibers

**FIGURE 8.13** Portions of two motor units. Muscle fibers within a motor unit are innervated by a single neuron and may be distributed throughout the muscle.

**PRACTICE**

14. Define *threshold stimulus.*
15. What is a motor unit?
16. Distinguish between a twitch and a sustained contraction.
17. What is recruitment?
18. How is muscle tone maintained?

## 8.5 | Smooth Muscle

The contractile mechanism of smooth muscle is essentially the same as for skeletal muscle. The cells of smooth muscle, however, have some important structural and functional differences from the other types of muscle.

### Smooth Muscle Fibers

Recall from chapter 5 (p. 121) that smooth muscle cells are elongated, with tapering ends. Smooth muscle cells contain filaments of actin and myosin in myofibrils that extend the lengths of the cells, but these filaments are organized differently and more randomly than those in skeletal muscle. Therefore, smooth muscle cells lack striations (and appear "smooth" under the microscope). The sarcoplasmic reticulum in these cells is not well developed.

The two major types of smooth muscle are multiunit and visceral. In **multiunit smooth muscle,** the muscle fibers are separate rather than organized into sheets. Smooth muscle of this type is found in the irises of the eyes and in the walls of blood vessels. Typically, multiunit smooth muscle tissue contracts only in response to stimulation by neurons or certain hormones.

**Visceral smooth muscle** is composed of sheets of spindle-shaped cells in close contact with one another (see fig. 5.23, p. 122). This more common type of smooth muscle is found in the walls of hollow organs, such as the stomach, intestines, urinary bladder, and uterus.

Fibers of visceral smooth muscle can stimulate each other. When one fiber is stimulated, the impulse moving over its surface may excite adjacent fibers, which in turn stimulate still others. Visceral smooth muscle also displays *rhythmicity,* a pattern of repeated contractions. Rhythmicity is due to self-exciting fibers that deliver spontaneous impulses periodically into surrounding muscle tissue. These two features—transmission of impulses from cell to cell and rhythmicity—are largely responsible for the wavelike motion, called **peristalsis,** that helps force the contents of certain tubular organs along their lengths. Peristalsis occurs, for example, in the intestines.

### Smooth Muscle Contraction

Smooth muscle contraction resembles skeletal muscle contraction in a number of ways. Both mechanisms include reactions of actin and myosin, both are triggered by membrane impulses and an increase in intracellular calcium ions, and both use energy from ATP. However, these two types of muscle tissue also have significant differences.

Recall that acetylcholine is the neurotransmitter in skeletal muscle. Two neurotransmitters affect smooth muscle—acetylcholine and norepinephrine. Each of these neurotransmitters stimulates contractions in some smooth muscle and inhibits contractions in other smooth muscle (see chapter 9, p. 266). Also, a number of hormones affect smooth muscle, stimulating contractions in some cases and altering the degree of response to neurotransmitters in others.

Smooth muscle is slower to contract and to relax than skeletal muscle. On the other hand, smooth muscle can maintain a forceful contraction longer with a given amount of ATP. Also, unlike skeletal muscle, smooth muscle fibers can change length without changing tautness. As a result, smooth muscle in the stomach and intestinal walls can stretch as these organs fill, yet maintain the pressure inside these organs.

**PRACTICE**

19. Describe two major types of smooth muscle.
20. What special characteristics of visceral smooth muscle make peristalsis possible?
21. How does smooth muscle contraction differ from skeletal muscle contraction?

## 8.6 | Cardiac Muscle

Cardiac muscle is found only in the heart. Its mechanism of contraction is essentially the same as that of skeletal and smooth muscle, but with some important differences.

Cardiac muscle is composed of branching, striated cells interconnected in three-dimensional networks (see fig. 5.24, p. 123). Each cell has many filaments of actin and myosin, organized similarly to those in skeletal muscle. A cardiac muscle cell also has a sarcoplasmic reticulum, many mitochondria, and a system of transverse tubules. However, the cisternae of cardiac muscle fibers are less well developed and store less calcium than those of skeletal muscle. On the other hand, the transverse tubules of cardiac muscle are larger, and they release many calcium ions into the sarcoplasm in response to muscle impulses. This extra calcium from the transverse tubules comes from the extracellular fluid and causes cardiac muscle twitches to be longer than skeletal muscle twitches.

The opposing ends of cardiac muscle cells are connected by structures called *intercalated discs.* These are elaborate junctions between cardiac muscle cell membranes. Intercalated discs allow muscle impulses to pass freely so that they travel rapidly from cell to cell, triggering contraction. The discs help to join cells and to transmit the force of contraction from cell to cell. Thus, when one portion of the cardiac muscle network is stimulated, the resulting impulse passes to the other parts of the network, and the whole structure contracts as a functional unit.

Cardiac muscle is also self-exciting and rhythmic. Consequently, a pattern of contraction and relaxation repeats, causing the rhythmic contractions of the heart.

Table 8.3 summarizes the characteristics of the three types of muscle tissue. Genetics Connection 8.1 considers several inherited diseases that affect the muscular system.

**PRACTICE**

22. How is cardiac muscle similar to smooth muscle?
23. How is cardiac muscle similar to skeletal muscle?
24. What is the function of intercalated discs?
25. What characteristic of cardiac muscle contracts the heart as a unit?

## 8.7 | Skeletal Muscle Actions

Skeletal muscles provide a variety of body movements, as described in chapter 7 (pp. 177–180). Each muscle's movement depends largely on the kind of joint it is associated with and the way the muscle attaches on either side of that joint.

### Origin and Insertion

Recall that bones forming movable joints function as levers (see chapter 7, p. 149). One end of a skeletal muscle usually fastens to a relatively immovable or fixed part at a movable joint, and the other end connects to a movable part on the other side of that joint. The less movable end of the muscle is called its **origin** (or′ĭ-jin), and the more movable end is its **insertion** (in-ser′shun). When a muscle contracts, its insertion is pulled toward its origin.

Some muscles have more than one origin or insertion. The *biceps brachii* in the arm, for example, has two origins. This is reflected in the name *biceps,* which means "two heads." (Note: The head of a muscle is the part nearest its origin.) One head of the muscle attaches to the coracoid process of the scapula, and the other head arises from a tubercle above the glenoid cavity of the scapula. The muscle extends along the anterior surface of the humerus and is inserted by means of a tendon on the radial tuberosity of the radius. When the biceps brachii contracts, its insertion is pulled toward its origin, and the forearm flexes at the elbow (fig. 8.14).

The movements termed *flexion* and *extension* describe changes in the angle between bones that meet at a joint. For example, flexion of the elbow refers to a movement of the forearm that bends the elbow, or decreases the angle. Alternatively, one could say that

**TABLE 8.3 Types of Muscle Tissue**

| | Skeletal | Smooth | Cardiac |
|---|---|---|---|
| *Major Location* | Skeletal muscles | Walls of hollow viscera, blood vessels | Wall of the heart |
| *Major Function* | Movement of bones at joints, maintenance of posture | Movement of viscera, peristalsis, vasoconstriction | Pumping action of the heart |
| *Cellular Characteristics* | | | |
| Striations | Present | Absent | Present |
| Nucleus | Many nuclei | Single nucleus | Single nucleus |
| Special features | Well-developed transverse tubule system | Lacks transverse tubules | Well-developed transverse tubule system; intercalated discs separating adjacent cells |
| *Mode of Control* | Voluntary | Involuntary | Involuntary |
| *Contraction Characteristics* | Contracts and relaxes rapidly | Contracts and relaxes slowly; self-exciting; rhythmic | Network of cells contracts as a unit; self-exciting; rhythmic |

GENETICS CONNECTION **8.1**

## Inherited Diseases of Muscle

Several inherited conditions affect muscle tissue. These disorders differ in the nature of the genetic defect, the type of protein that is abnormal in form or function, and the muscles that are impaired.

### The Muscular Dystrophies—Missing Proteins

A muscle cell is packed with filaments of actin and myosin. Much less abundant, but no less important, is a protein called *dystrophin*. It holds skeletal muscle cells together by linking actin in the cell to glycoproteins in the cell membrane, which helps attach the cell to the extracellular matrix.

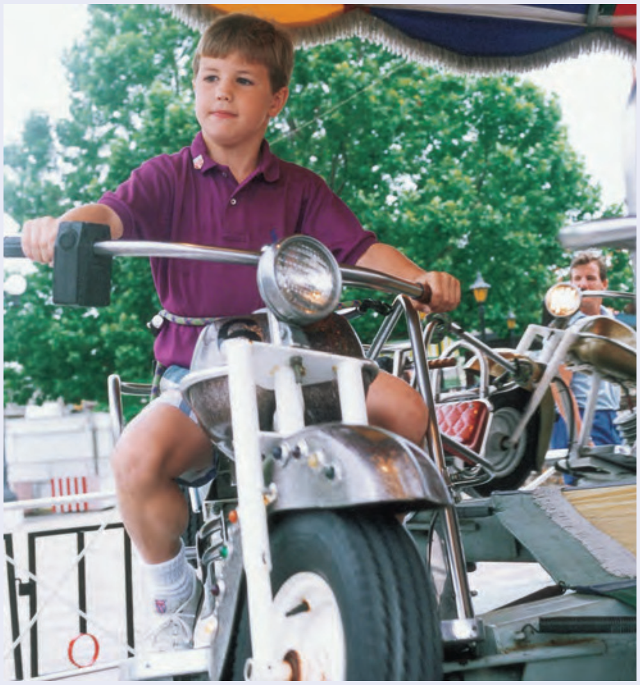


**FIGURE 8B** This young man has Duchenne muscular dystrophy. The condition has not yet severely limited his activities, but he shows the hypertrophied (overdeveloped) calf muscles that result from his inability to rise from a sitting position the usual way—an early sign of the illness.

Missing or abnormal dystrophin or the glycoproteins cause muscular dystrophies. These illnesses vary in severity and age of onset, but in all cases, muscles weaken and degenerate. Eventually, fat and connective tissue replace muscle.

Duchenne muscular dystrophy (DMD) is the most severe type of the illness (fig. 8B). Symptoms begin by age five and affect only boys. By age thirteen, the person cannot walk, and by early adulthood he usually dies from failure of the respiratory muscles. In DMD, dystrophin is absent or shortened. In Becker muscular dystrophy, symptoms begin in early adulthood, are less severe, and result from underproduction of dystrophin. An experimental genetic therapy produces nearly full-length dystrophin by skipping over the part of the gene that includes the mutation.

### Charcot-Marie-Tooth Disease—A Duplicate Gene

Charcot-Marie-Tooth disease causes a slowly progressing weakness in the muscles of the hands and feet and a decrease in tendon reflexes in these parts. In this illness, an extra gene impairs the insulating sheath around affected nerve cells, so that nerve cells cannot adequately stimulate muscles. Physicians perform two tests—electromyography and nerve conduction velocity—to diagnose Charcot-Marie-Tooth disease. It is also possible to test for gene mutations to confirm a diagnosis based on symptoms.

### Hereditary Idiopathic Dilated Cardiomyopathy—A Tiny Glitch

This very rare inherited form of heart failure usually begins in a person's forties and is lethal in 50% of cases within five years of diagnosis, unless a heart transplant can be performed. The condition is caused by a mutation in a gene that encodes a form of actin found only in cardiac muscle. The mutation disturbs actin's ability to anchor to the Z lines in heart muscle cells, preventing actin from effectively transmitting the force of contraction. As a result, the heart chambers enlarge and eventually fail.

flexion of the elbow results from the action of the biceps brachii on the radius of the forearm.

Because students (and patients) often find it helpful to think of movements in terms of the specific actions of the muscles involved, we may also describe flexion and extension in these terms. Thus, the action of the biceps brachii may be described as "flexion of the forearm at the elbow," and the action of the quadriceps group as "extension of the leg at the knee." We believe this occasional departure from strict anatomical terminology may ease understanding and learning.

## Interaction of Skeletal Muscles

Skeletal muscles almost always function in groups. Consequently, a particular body movement requires more than contracting a single muscle; instead, after learning to make a particular movement, the person initiates the

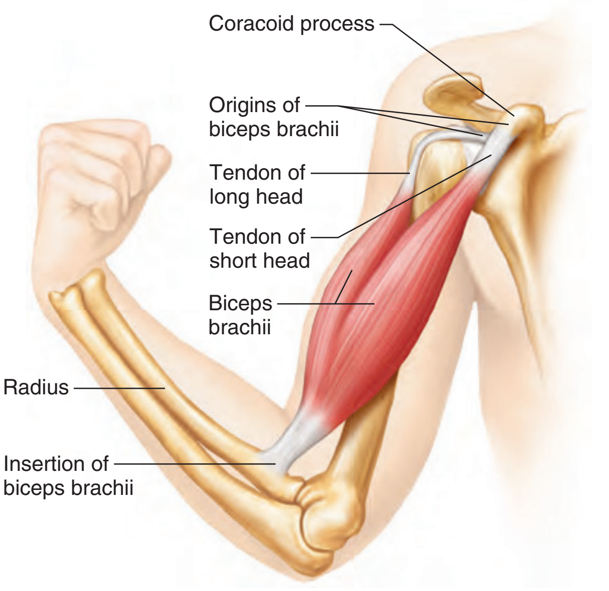


**FIGURE 8.14** The biceps brachii has two heads that originate on the scapula. A tendon inserts this muscle on the radius.

movement consciously, and the nervous system stimulates the appropriate group of muscles.

A number of terms describe the roles of muscles in performing particular actions. An *agonist* (ag′o-nist) causes an action while an *antagonist* (an-tag′o-nist) works against the action. In the example of elbow flexion, biceps brachii is the agonist for flexion and the antagonist to that movement is triceps brachii. Note that the role of a muscle is dependent on the movement, because in the opposite example of elbow extension, triceps brachii is the agonist and biceps brachii is the antagonist.

In most cases other muscles, called *synergists*, contribute to an action by helping the agonist. Again, however, the relationship between muscles depends on the action. For example, pectoralis major, a chest muscle, and latissimus dorsi, a back muscle, are synergistic for medial rotation of the arm. However, they are antagonistic to each other for flexion and extension of the shoulder. Similarly, two muscles on the lateral forearm, flexor carpi radialis and extensor carpi radialis longus, are synergistic for abduction of the hand, yet they are antagonistic for flexion and extension of the wrist. Thus, any role of a muscle must be learned in the context of a particular movement.

The term *agonist* is often used interchangeably with *prime mover* (prīm moov′er), but in many applications the term *prime mover* refers to an agonist that provides most of the force for a movement when more than one muscle contributes.

If both an agonist and its antagonist contract simultaneously with equal force, the part they act upon remains rigid, or fixed. Smooth body movements depend on antagonists contracting somewhat, then giving way to an action whenever agonists contract. Once again, the nervous system controls these complex actions.

## PRACTICE

26. Distinguish between the origin and the insertion of a muscle.
27. Define *agonist*.
28. What is the function of a synergist? an antagonist?

## 8.8 | Major Skeletal Muscles

This section discusses the locations, actions, and attachments of some of the major skeletal muscles. (Figures 8.15 and 8.16 and reference plates 1 and 2, pp. 32–33, show the locations of the superficial skeletal muscles—those near the surface.)

The names of these muscles often describe them. A name may indicate a muscle's relative size, shape, location, action, number of attachments, or the direction of its fibers, as in the following examples:

| | |
|---|---|
| **pectoralis major** | Of large size (major) and located in the pectoral region (chest). |
| **deltoid** | Shaped like a delta or triangle. |
| **extensor digitorum** | Extends the digits (fingers or toes). |
| **biceps brachii** | Having two heads (biceps) or points of origin and located in the brachium (arm). |
| **sternocleidomastoid** | Attached to the sternum, clavicle, and mastoid process. |
| **external oblique** | Located near the outside, with fibers that run obliquely (in a slanting direction). |

Note that in the anatomical position some actions have already occurred, such as supination of the forearm and hand, extension of the elbow, and extension of the knee. The muscle actions described in the following section consider the entire range of movement at each joint, and do not presume that the starting point is the anatomical position.

Some muscles have more than one origin or more than one insertion. The wide range of attachments of some of the larger muscles has the effect of giving those muscles different, sometimes opposing actions, depending on which portion of the muscle is active. Many of these cases are identified in the appropriate sections and tables.

### Muscles of Facial Expression

A number of small muscles that lie beneath the skin of the face and scalp enable us to communicate feelings through facial expression (fig. 8.17*a*). Many of these muscles, located around the eyes and mouth, are

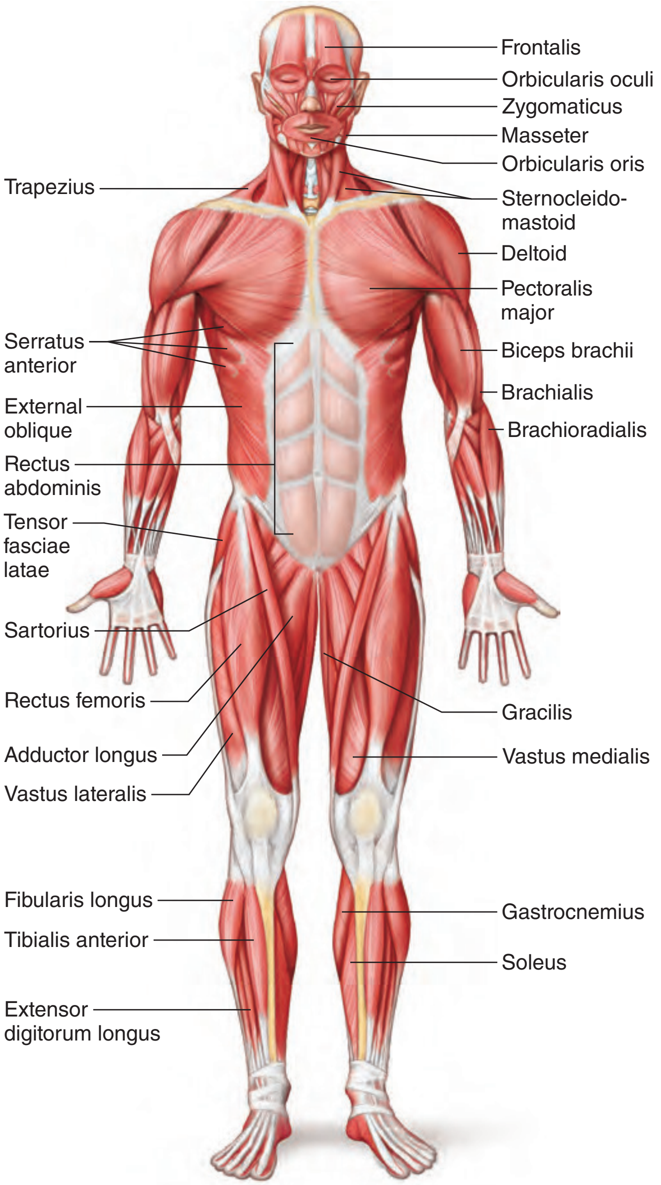

Frontalis
Orbicularis oculi
Zygomaticus
Masseter
Orbicularis oris
Trapezius
Sternocleido-mastoid
Deltoid
Pectoralis major
Serratus anterior
Biceps brachii
Brachialis
External oblique
Brachioradialis
Rectus abdominis
Tensor fasciae latae
Sartorius
Rectus femoris
Gracilis
Adductor longus
Vastus medialis
Vastus lateralis
Fibularis longus
Gastrocnemius
Tibialis anterior
Soleus
Extensor digitorum longus

**FIGURE 8.15** Anterior view of superficial skeletal muscles.

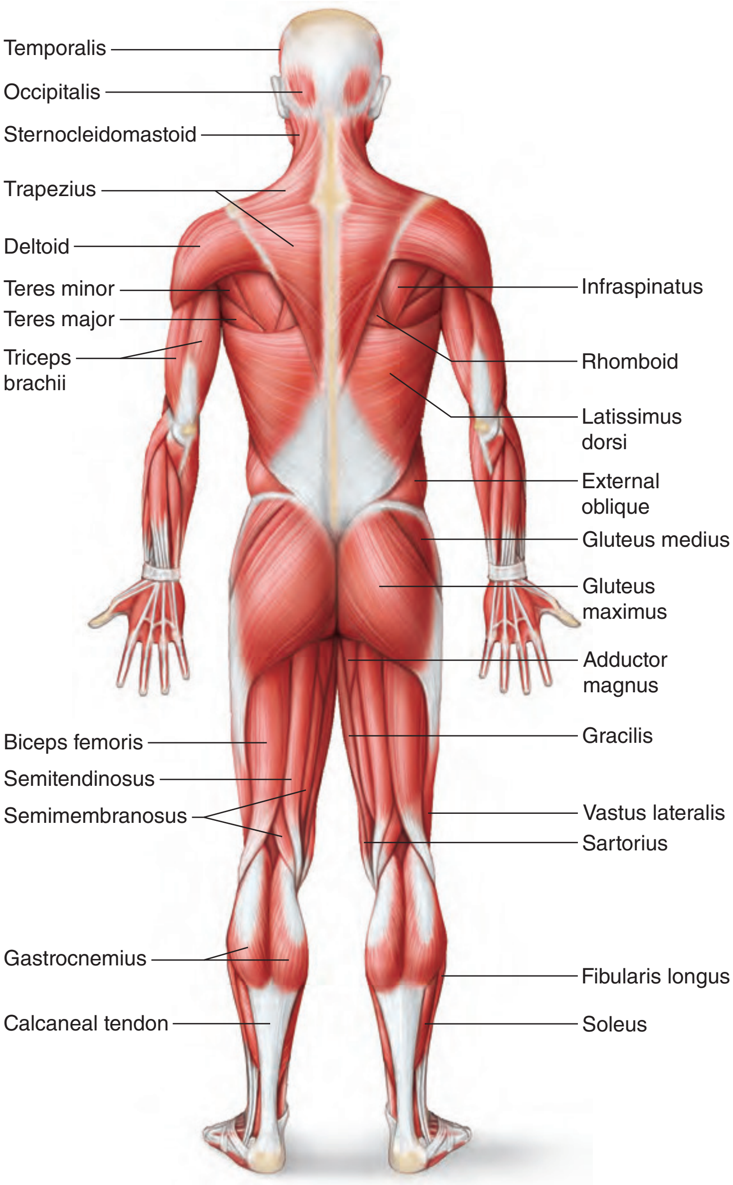

Temporalis
Occipitalis
Sternocleidomastoid
Trapezius
Deltoid
Teres minor
Infraspinatus
Teres major
Triceps brachii
Rhomboid
Latissimus dorsi
External oblique
Gluteus medius
Gluteus maximus
Adductor magnus
Biceps femoris
Gracilis
Semitendinosus
Semimembranosus
Vastus lateralis
Sartorius
Gastrocnemius
Fibularis longus
Calcaneal tendon
Soleus

**FIGURE 8.16** Posterior view of superficial skeletal muscles.

responsible for such expressions as surprise, sadness, anger, fear, disgust, and pain. As a group, the muscles of facial expression join the bones of the skull to connective tissue in various regions of the overlying skin. They include:

*epicranius* (ep″ĭ-kra′ne-us) Composed of two parts, the *frontalis* (frun-ta′lis) and the *occipitalis* (ok-sip″ĭ-ta′lis)
*orbicularis oculi* (or-bik′u-la-rus ok′u-li)
*orbicularis oris* (or-bik′u-la-rus o′ris)
*buccinator* (buk′sĭ-na″tor)
*zygomaticus* (zi″go-mat′ik-us)
*platysma* (plah-tiz′mah)

Table 8.4 lists the origins, insertions, and actions of the muscles of facial expression. Chapter 10 (pp. 289–291) describes the muscles that move the eyes.

**FACTS OF LIFE** The human body has more than 600 distinct skeletal muscles. The face alone includes 60 muscles, more than 40 of which are used to frown, and 20 to smile. Thinner than a thread and barely visible, the stapedius in the middle ear is the body's smallest muscle. In contrast is the gluteus maximus, the largest muscle, located in the buttock. The sartorius, which pulls on the leg just below the knee, is the longest muscle in the body.

## Muscles of Mastication

Muscles attached to the mandible produce chewing movements. Two pairs of these muscles elevate the mandible, a motion used in biting. These muscles are the *masseter* (mas-se′ter) and the *temporalis* (tem-po-ra′lis) (fig. 8.17*a*). Table 8.5 lists the origins, insertions, and actions of the muscles of mastication.

> Grinding the teeth, a common response to stress, may strain the temporomandibular joint—the articulation between the mandibular condyle of the mandible and the mandibular fossa of the temporal bone. This condition, called temporomandibular joint syndrome (TMJ syndrome), may produce headache, earache, and pain in the jaw, neck, or shoulder.

## Muscles That Move the Head

Head movements result from the actions of paired muscles in the neck and upper back. These muscles flex, extend, and rotate the head. Some muscles elevate the rib cage during forceful breathing. They include (see figs. 8.17*b* and 8.19):

*sternocleidomastoid* (ster″no-kli″do-mas′toid)
*splenius capitis* (sple′ne-us kap′ĭ-tis)
*semispinalis capitis* (sem″e-spi-na′lis kap′ĭ-tis)
*scalenes* (ska′lēnz)

Table 8.6 lists the origins, insertions, and actions of muscles that move the head.

### TABLE 8.4 Muscles of Facial Expression APR

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Epicranius | Occipital bone | Skin around eye | Elevates eyebrow |
| Orbicularis oculi | Maxillary and frontal bones | Skin around eye | Closes eye |
| Orbicularis oris | Muscles near the mouth | Skin of lips | Closes and protrudes lips |
| Buccinator | Alveolar processes of maxilla and mandible | Orbicularis oris | Compresses cheeks |
| Zygomaticus | Zygomatic bone | Skin and muscle at corner of mouth | Elevates corner of mouth |
| Platysma | Fascia in upper chest | Mandible | Depresses lower lip and angle of mouth |

### TABLE 8.5 Muscles of Mastication APR

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Masseter | Zygomatic arch | Posterior lateral surface of mandible | Elevates and protracts mandible |
| Temporalis | Temporal bone | Coronoid process of mandible | Elevates and retracts mandible |

### TABLE 8.6 Muscles That Move the Head APR

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Sternocleidomastoid | Manubrium of sternum and medial clavicle | Mastoid process of temporal bone | Each laterally flexes head to the same side, rotates head to the opposite side. Together they flex the head and neck forward; also aid in forceful inhalation. |
| Splenius capitis | Spinous processes of lower cervical and upper thoracic vertebrae | Mastoid process of temporal bone | Rotates head, laterally flexes head, brings head into an upright position |
| Semispinalis capitis | Transverse processes of lower cervical and upper thoracic vertebrae | Occipital bone | Extends head and neck, laterally flexes head, rotates head |
| Scalenes | Transverse processes of cervical vertebrae | Superior and lateral surfaces of first two ribs | Flex head and neck, elevate first two ribs during forceful inhalation |

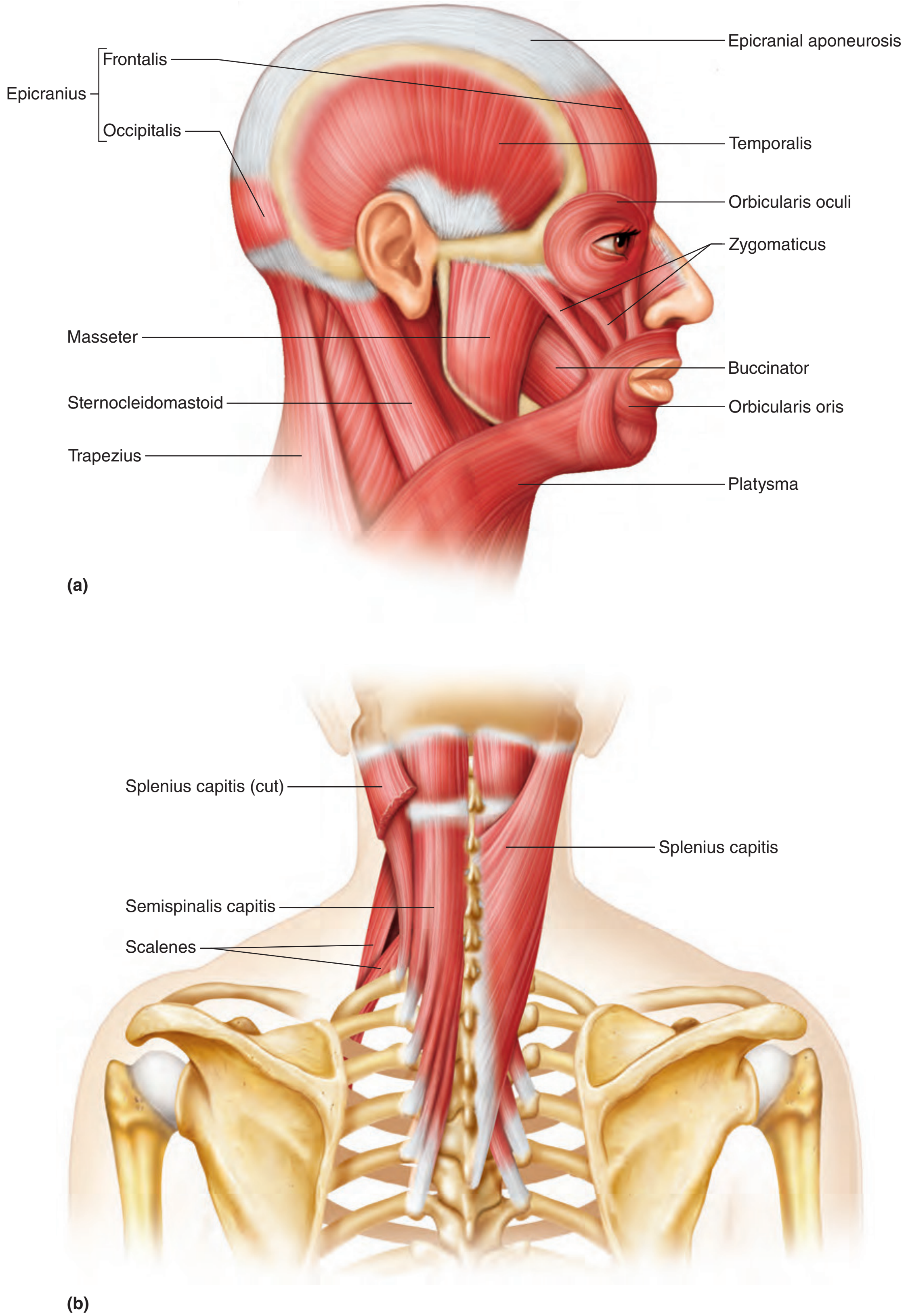

Epicranius
Frontalis
Occipitalis
Epicranial aponeurosis
Temporalis
Orbicularis oculi
Zygomaticus
Masseter
Buccinator
Orbicularis oris
Sternocleidomastoid
Trapezius
Platysma
(a)
Splenius capitis (cut)
Splenius capitis
Semispinalis capitis
Scalenes
(b)

**FIGURE 8.17** APR Muscles of the face and neck. **(a)** Muscles of facial expression and mastication. **(b)** Posterior view of muscles that move the head.

## Muscles That Move the Pectoral Girdle

The muscles that move the pectoral girdle are closely associated with those that move the arm. A number of these chest and shoulder muscles connect the scapula to nearby bones and move the scapula upward, downward, forward, and backward. They include (figs. 8.18 and 8.19):

*trapezius* (trah-pe′ze-us)
*rhomboid major* (rom-boid′)
*levator scapulae* (le-va′tor scap′u-lē)
*serratus anterior* (ser-ra′tus an-te′re-or)
*pectoralis minor* (pek″to-ra′lis)

Table 8.7 lists the origins, insertions, and actions of the muscles that move the pectoral girdle.

## Muscles That Move the Arm

The arm is one of the more freely movable parts of the body. Muscles that connect the humerus to various regions of the pectoral girdle, ribs, and vertebral column

**TABLE 8.7** **Muscles That Move the Pectoral Girdle** APR

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Trapezius | Occipital bone and spinous processes of cervical and thoracic vertebrae | Clavicle; spine and acromion process of scapula | Rotates and retracts scapula<br>Superior portion elevates scapula, inferior portion depresses scapula |
| Rhomboid major | Spinous processes of upper thoracic vertebrae | Medial border of scapula | Elevates and retracts scapula |
| Levator scapulae | Transverse processes of cervical vertebrae | Medial border of scapula | Elevates scapula |
| Serratus anterior | Anterior surfaces of upper ribs | Medial border of scapula | Protracts and rotates scapula |
| Pectoralis minor | Anterior surfaces of ribs 3–5 | Coracoid process of scapula | Depresses and protracts scapula, elevates ribs during forceful inhalation |

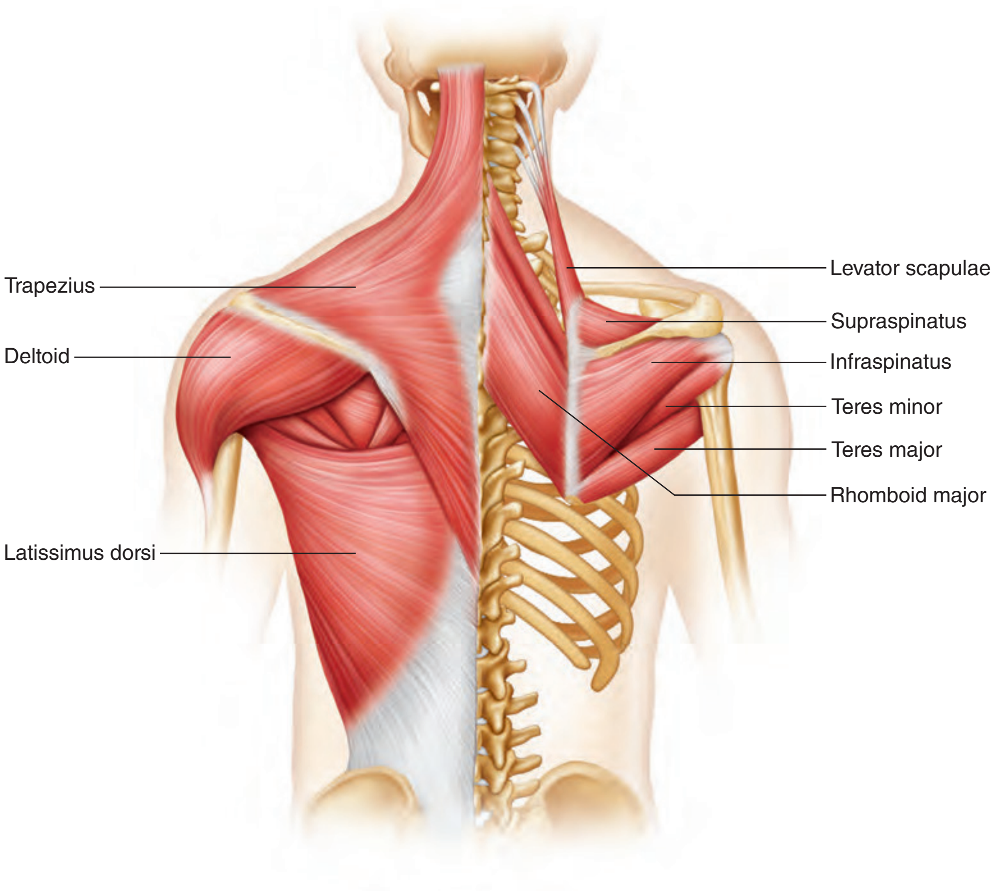


**FIGURE 8.18** APR Muscles of the posterior shoulder. The right trapezius is removed to show underlying muscles.

make these movements possible (figs. 8.18, 8.19, 8.20, and 8.21). These muscles can be grouped according to their primary actions—flexion, extension, abduction, and rotation—as follows:

**Flexors**
*coracobrachialis* (kor″ah-ko-bra′ke-al-is)
*pectoralis major* (pek″to-ra′lis)

**Extensors**
*teres major* (te′rēz)
*latissimus dorsi* (lah-tis′ĭ-mus dor′si)

**Abductors**
*supraspinatus* (su″prah-spi′na-tus)
*deltoid* (del′toid)

**Rotators**
*subscapularis* (sub-scap′u-lar-is)
*infraspinatus* (in″frah-spi′na-tus)
*teres minor* (te′rēz)

The movements of flexion and extension of the shoulder may be less obvious than at other joints. Movements of the arm forward and upward flex the shoulder, and the opposite movements extend it. Table 8.8 lists the origins, insertions, and actions of muscles that move the arm.

## Muscles That Move the Forearm

Muscles that connect the radius or ulna to the humerus or pectoral girdle produce most of the forearm movements. A group of muscles located along the anterior surface of the humerus flexes the elbow, and a single posterior muscle extends this joint. Other muscles move the radioulnar joint and rotate the forearm.

Muscles that move the forearm include (figs. 8.20, 8.21, and 8.22):

**Flexors**
*biceps brachii* (bi′seps bra′ke-i)
*brachialis* (bra′ke-al-is)
*brachioradialis* (bra″ke-o-ra″de-a′lis)

**Extensor**
*triceps brachii* (tri′seps bra′ke-i)

**Rotators**
*supinator* (su′pĭ-na-tor)
*pronator teres* (pro-na′tor te′rēz)
*pronator quadratus* (pro-na′tor kwod-ra′tus)

Table 8.9 lists the origins, insertions, and actions of muscles that move the forearm.

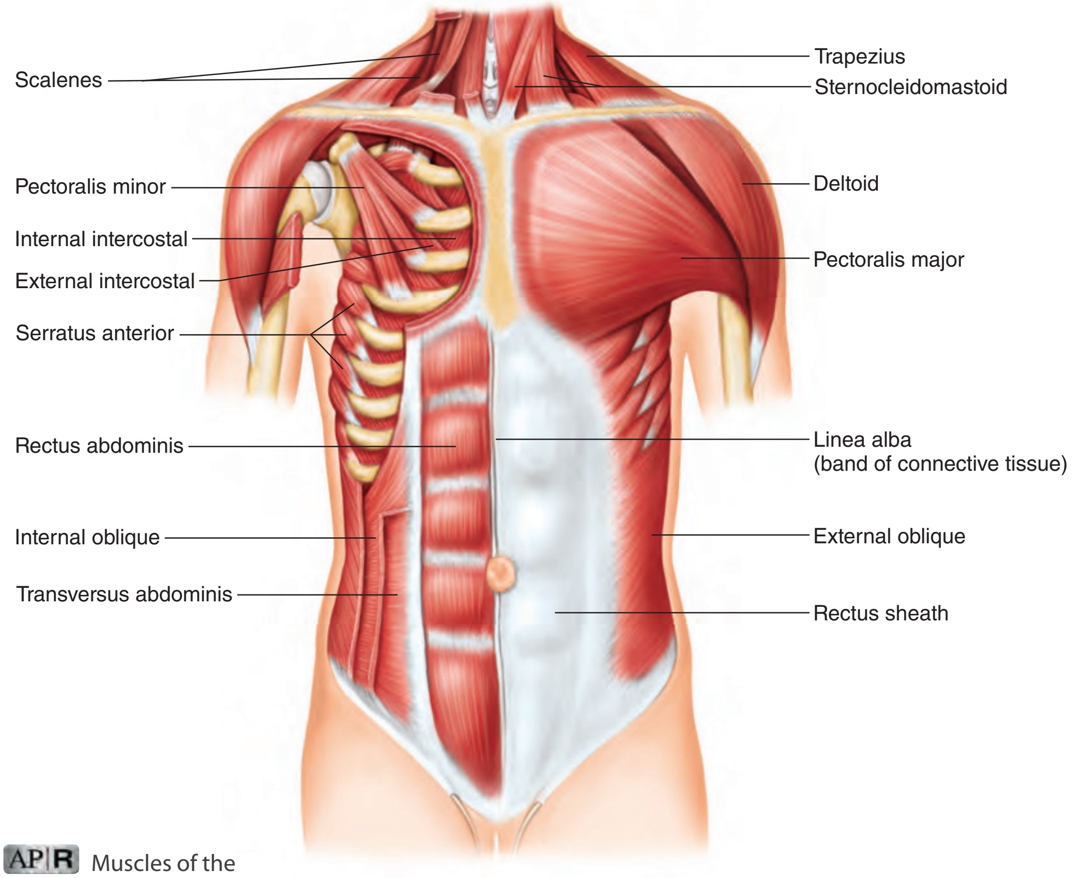

Scalenes
Trapezius
Sternocleidomastoid
Pectoralis minor
Deltoid
Internal intercostal
Pectoralis major
External intercostal
Serratus anterior
Rectus abdominis
Linea alba
(band of connective tissue)
Internal oblique
External oblique
Transversus abdominis
Rectus sheath

**FIGURE 8.19** APR Muscles of the anterior chest and abdominal wall. The right pectoralis major is removed to show the pectoralis minor.

## TABLE 8.8 Muscles That Move the Arm APR

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Coracobrachialis | Coracoid process of scapula | Medial midshaft of humerus | Flexes arm at shoulder, adducts arm |
| Pectoralis major | Clavicle, sternum, and costal cartilages of upper ribs | Intertubercular sulcus of humerus | Flexes arm at shoulder, adducts and medially rotates arm |
| Teres major | Lateral border of scapula | Intertubercular sulcus of humerus | Extends arm at shoulder, adducts and medially rotates arm |
| Latissimus dorsi | Spinous processes of lower thoracic and lumbar vertebrae, iliac crest, and lower ribs | Intertubercular sulcus of humerus | Extends arm at shoulder, adducts and medially rotates arm |
| Supraspinatus | Supraspinous fossa of scapula | Greater tubercle of humerus | Abducts arm |
| Deltoid | Acromion process, spine of scapula, and clavicle | Deltoid tuberosity of humerus | Lateral portion abducts arm<br>Anterior portion flexes arm at shoulder<br>Posterior portion extends arm at shoulder |
| Subscapularis | Anterior surface of scapula | Lesser tubercle of humerus | Rotates arm medially |
| Infraspinatus | Infraspinous fossa of scapula | Greater tubercle of humerus | Rotates arm laterally |
| Teres minor | Lateral border of scapula | Greater tubercle of humerus | Rotates arm laterally |

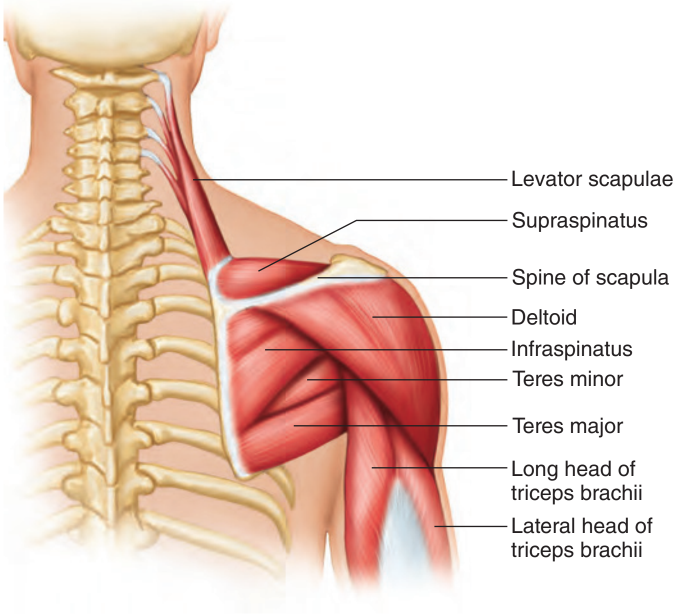

Levator scapulae
Supraspinatus
Spine of scapula
Deltoid
Infraspinatus
Teres minor
Teres major
Long head of triceps brachii
Lateral head of triceps brachii

**FIGURE 8.20** APR Muscles of the posterior surface of the scapula and arm.

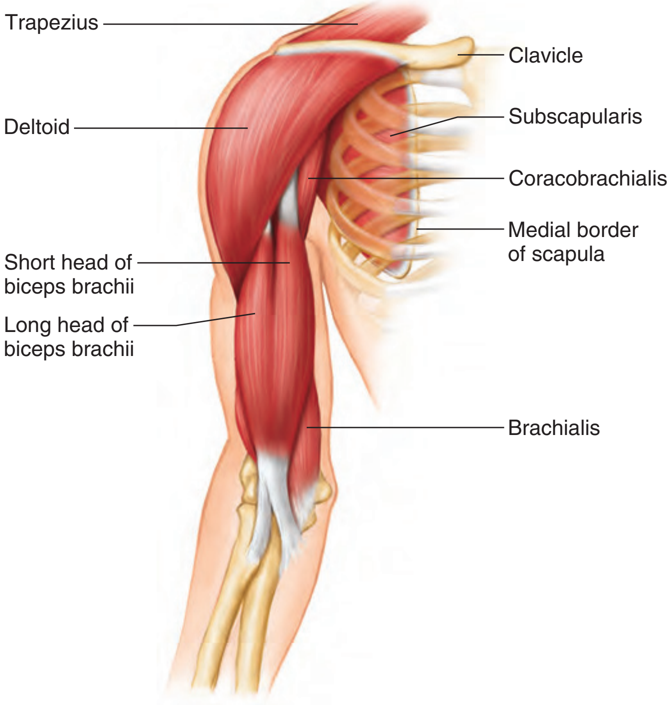

Trapezius
Clavicle
Subscapularis
Deltoid
Coracobrachialis
Medial border of scapula
Short head of biceps brachii
Long head of biceps brachii
Brachialis

**FIGURE 8.21** APR Muscles of the anterior shoulder and arm.

## Muscles That Move the Hand

Many muscles move the hand. They originate from the distal end of the humerus and from the radius and ulna. The two major groups of these muscles are flexors on the anterior side of the forearm and extensors on the posterior side. These muscles include (figs. 8.22 and 8.23):

**Flexors**

*flexor carpi radialis* (flex′sor kar-pi′ ra″de-a′lis)
*flexor carpi ulnaris* (flex′sor kar-pi′ ul-na′ris)
*palmaris longus* (pal-ma′ris long′gus)
*flexor digitorum profundus* (flex′sor dij″ĭ-to′rum pro-fun′dus)

**Extensors**

*extensor carpi radialis longus* (eks-ten′sor kar-pi′ ra″de-a′lis long′gus)
*extensor carpi radialis brevis* (eks-ten′sor kar-pi′ ra″de-a′lis brev′ĭs)
*extensor carpi ulnaris* (eks-ten′sor kar-pi′ ul-na′ris)
*extensor digitorum* (eks-ten′sor dij″ĭ-to′rum)

Table 8.10 lists the origins, insertions, and actions of muscles that move the hand.

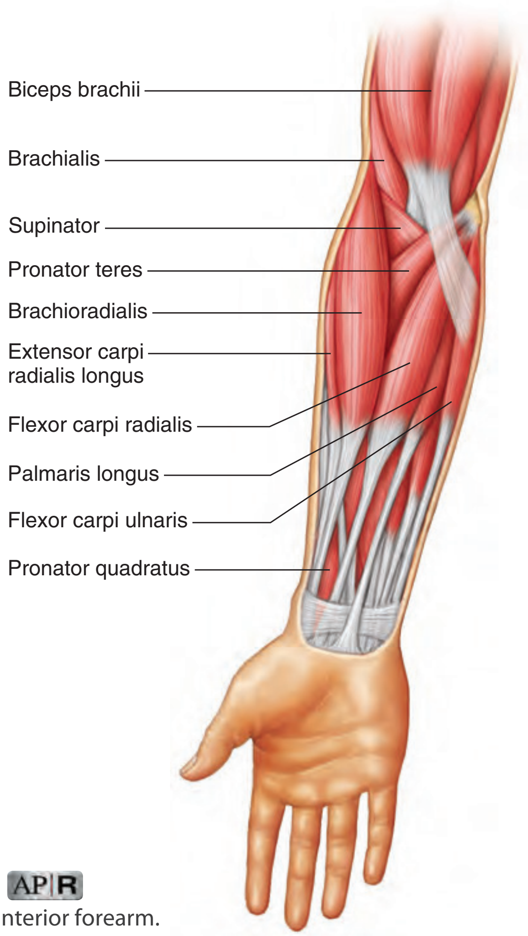


**FIGURE 8.22** APR
Muscles of the anterior forearm.

**TABLE 8.9 Muscles That Move the Forearm** APR

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Biceps brachii | Coracoid process and tubercle above glenoid cavity of scapula | Radial tuberosity of radius | Flexes forearm at elbow, supinates forearm and hand |
| Brachialis | Anterior surface of humerus | Coronoid process of ulna | Flexes forearm at elbow |
| Brachioradialis | Distal lateral end of humerus | Lateral surface of radius above styloid process | Flexes forearm at elbow |
| Triceps brachii | Tubercle below glenoid cavity and lateral and posterior surfaces of humerus | Olecranon process of ulna | Extends forearm at elbow |
| Supinator | Lateral epicondyle of humerus and proximal ulna | Anterior and lateral surface of radius | Supinates forearm and hand |
| Pronator teres | Medial epicondyle of humerus and coronoid process of ulna | Lateral surface of radius | Pronates forearm and hand |
| Pronator quadratus | Anterior distal end of ulna | Anterior distal end of radius | Pronates forearm and hand |

**TABLE 8.10 Muscles That Move the Hand**

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Flexor carpi radialis | Medial epicondyle of humerus | Base of second and third metacarpals | Flexes wrist, abducts hand |
| Flexor carpi ulnaris | Medial epicondyle of humerus and olecranon process of ulna | Carpal and metacarpal bones | Flexes wrist, adducts hand |
| Palmaris longus | Medial epicondyle of humerus | Fascia of palm | Flexes wrist |
| Flexor digitorum profundus | Anterior and medial surface of ulna | Distal phalanges of fingers 2–5 | Flexes wrist and joints of fingers |
| Extensor carpi radialis longus | Lateral distal end of humerus | Base of second metacarpal | Extends wrist, abducts hand |
| Extensor carpi radialis brevis | Lateral epicondyle of humerus | Base of third metacarpal | Extends wrist, abducts hand |
| Extensor carpi ulnaris | Lateral epicondyle of humerus and proximal, posterior ulna | Base of fifth metacarpal | Extends wrist, adducts hand |
| Extensor digitorum | Lateral epicondyle of humerus | Posterior surface of phalanges in fingers 2–5 | Extends joints of fingers |

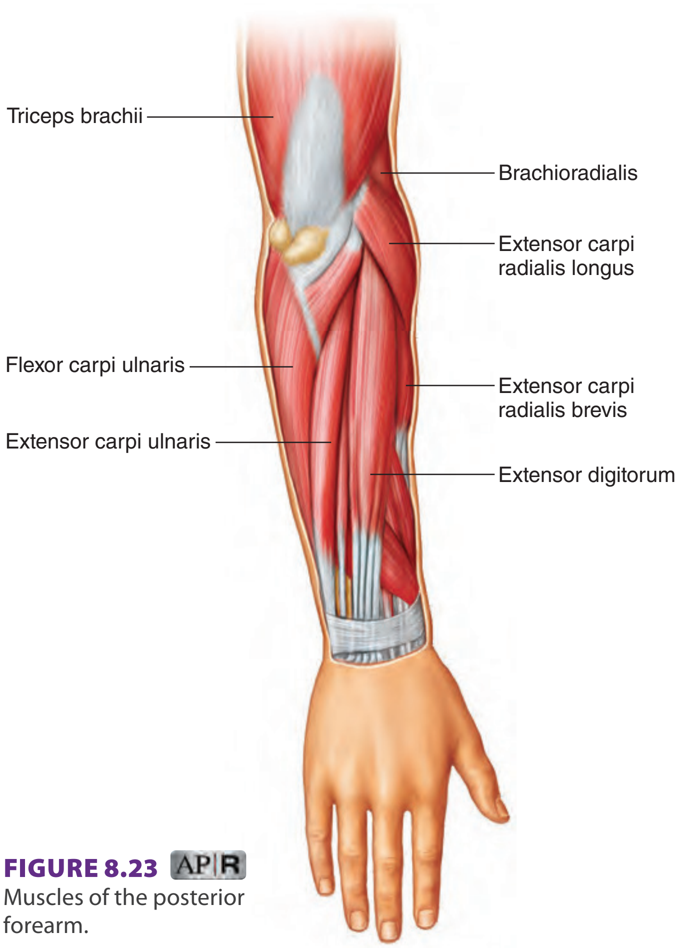


**FIGURE 8.23** APR
Muscles of the posterior forearm.

## Muscles of the Abdominal Wall

Bone supports the walls of the chest and pelvic regions, but not those of the abdomen. Instead, the anterior and lateral walls of the abdomen are composed of layers of broad, flattened muscles. These muscles connect the rib cage and vertebral column to the pelvic girdle. A band of tough connective tissue called the **linea alba** extends from the xiphoid process of the sternum to the pubic symphysis (see fig. 8.19). It is an attachment for some of the abdominal wall muscles. Another important attachment is the inguinal ligament, which extends from the anterior superior iliac spine to the pubis near the pubic symphysis.

Contraction of these muscles decreases the size of the abdominal cavity and increases the pressure inside. These actions help press air out of the lungs during forceful exhalation and aid in the movements of defecation, urination, vomiting, and childbirth.

The abdominal wall muscles include (see fig. 8.19):

*external oblique* (eks-ter′nal o-blēk′)
*internal oblique* (in-ter′nal o-blēk′)
*transversus abdominis* (trans-ver′sus ab-dom′ĭ-nis)
*rectus abdominis* (rek′tus ab-dom′ĭ-nis)

Table 8.11 lists the origins, insertions, and actions of muscles of the abdominal wall.

## Muscles of the Pelvic Floor

Two muscular sheets—a deeper **pelvic diaphragm** and a more superficial **urogenital diaphragm**—form the floor of the pelvis. The pelvic diaphragm spans the outlet of the pelvic cavity, and the urogenital diaphragm fills the space within the pubic arch (see fig. 7.29, p. 171). Just anterior to the anal canal, a deep central tendon serves as an attachment for a number of these muscles. The muscles of the male and female pelvic floors include (fig. 8.24):

**Pelvic diaphragm**
*levator ani* (le-va′tor ah-ni′)
*coccygeus* (kok-sij′e-us)

## TABLE 8.11 Muscles of the Abdominal Wall

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| External oblique | Outer surfaces of lower 8 ribs | Outer lip of iliac crest and linea alba | Compresses abdomen, flexes and rotates vertebral column |
| Internal oblique | Iliac crest and inguinal ligament | Lower 3–4 ribs, linea alba, and crest of pubis | Compresses abdomen, flexes and rotates vertebral column |
| Transversus abdominis | Costal cartilages of lower 6 ribs, processes of lumbar vertebrae, lip of iliac crest, and inguinal ligament | Linea alba and crest of pubis | Compresses abdomen, flexes and rotates vertebral column |
| Rectus abdominis | Crest of pubis and pubic symphysis | Xiphoid process of sternum and costal cartilages | Compresses abdomen, flexes vertebral column |

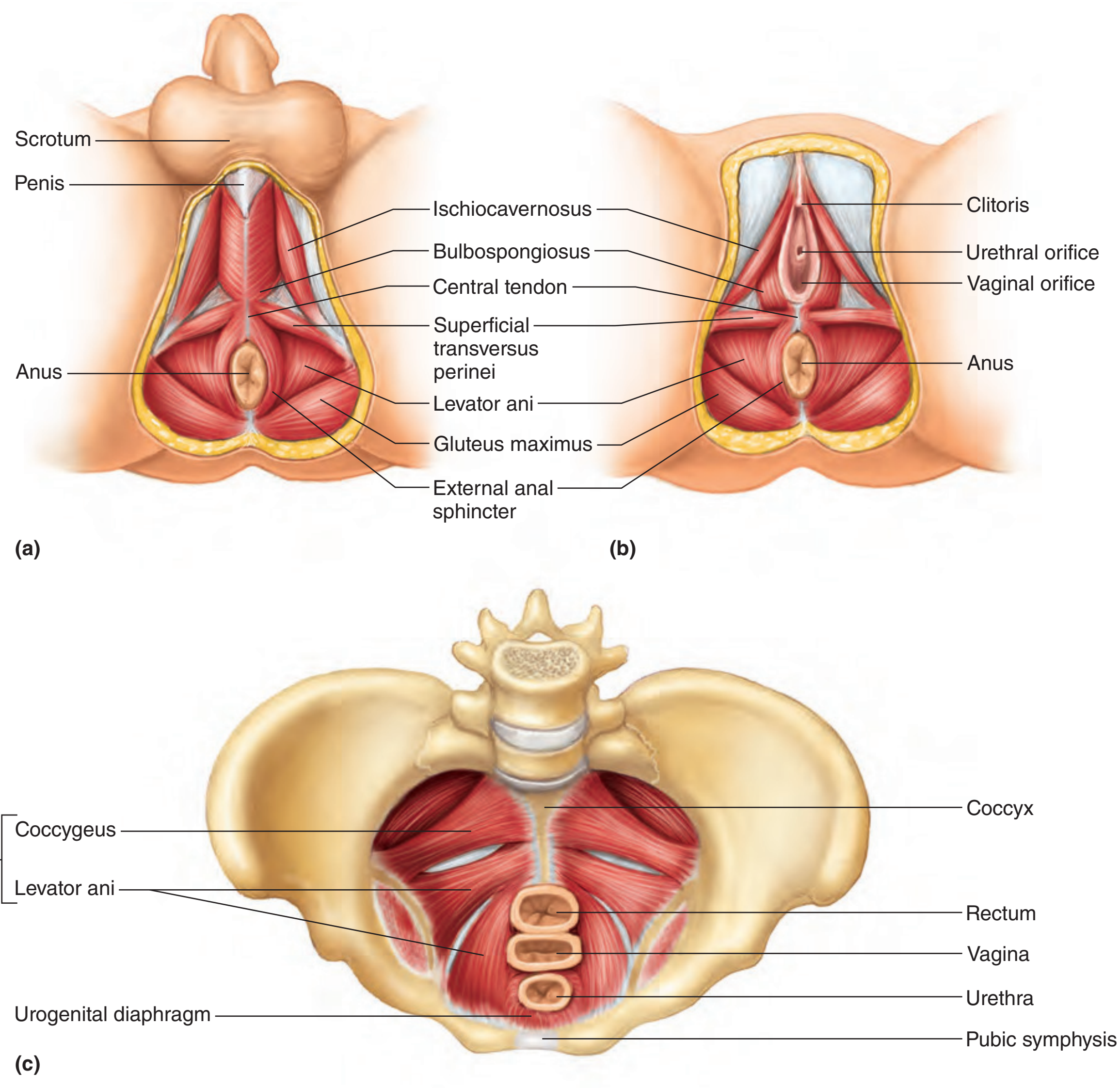

Scrotum
Penis
Anus
Ischiocavernosus
Bulbospongiosus
Central tendon
Superficial transversus perinei
Levator ani
Gluteus maximus
External anal sphincter
Clitoris
Urethral orifice
Vaginal orifice
Anus
(a)
(b)
Pelvic diaphragm
Coccygeus
Levator ani
Urogenital diaphragm
Coccyx
Rectum
Vagina
Urethra
Pubic symphysis
(c)

**FIGURE 8.24** APR External view of muscles of **(a)** the male pelvic floor and **(b)** the female pelvic floor. **(c)** Internal view of the female pelvic and urogenital diaphragms.

**Urogenital diaphragm**
*superficial transversus perinei* (su″per-fish′al
trans-ver′sus per″ĭ-ne′i)
*bulbospongiosus* (bul″bo-spon″je-o′sus)
*ischiocavernosus* (is″ke-o-kav″er-no′sus)

Table 8.12 lists the origins, insertions, and actions of pelvic floor muscles.

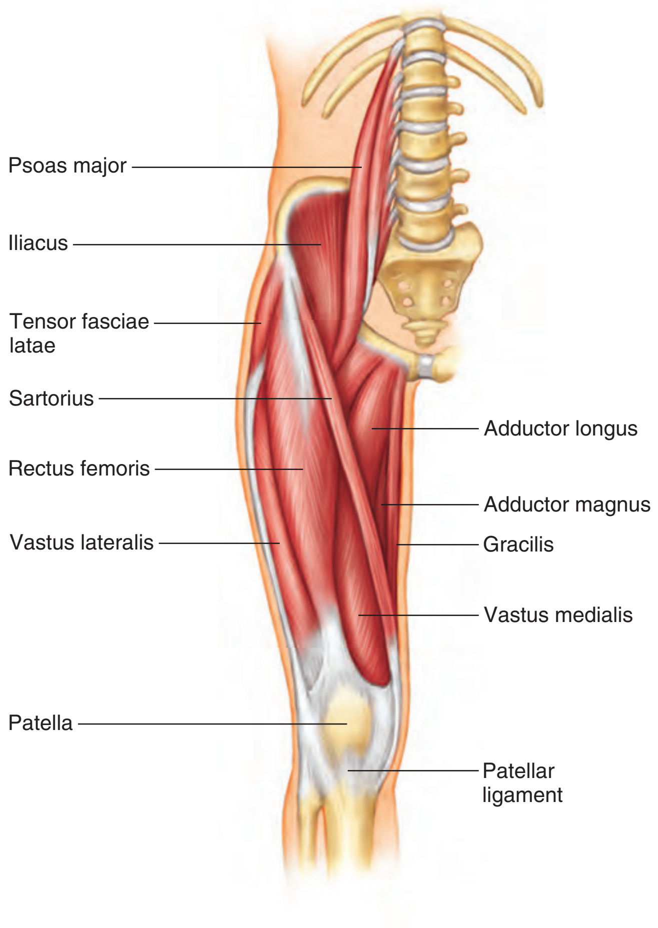

Psoas major
Iliacus
Tensor fasciae latae
Sartorius
Rectus femoris
Vastus lateralis
Patella
Adductor longus
Adductor magnus
Gracilis
Vastus medialis
Patellar ligament

**FIGURE 8.25** APR Muscles of the anterior right thigh. (Note that the vastus intermedius is a deep muscle not visible in this view.)

## Muscles That Move the Thigh

Muscles that move the thigh are attached to the femur and to some part of the pelvic girdle. These muscles are in anterior and posterior groups. Muscles of the anterior group primarily flex the thigh; those of the posterior group extend, abduct, or rotate the thigh. The muscles in these groups include (figs. 8.25, 8.26, and 8.27):

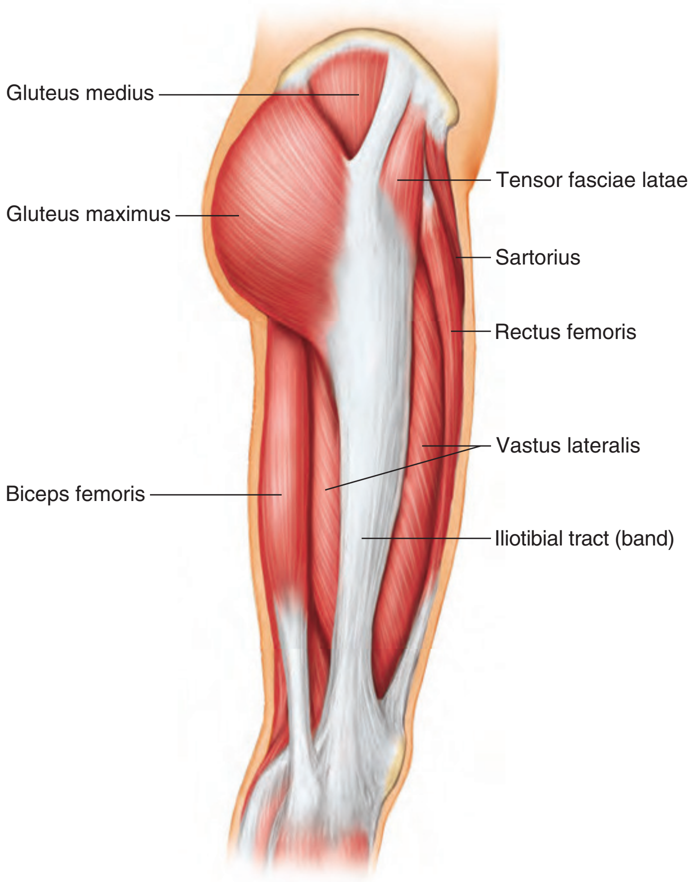

Gluteus medius
Gluteus maximus
Biceps femoris
Tensor fasciae latae
Sartorius
Rectus femoris
Vastus lateralis
Iliotibial tract (band)

**FIGURE 8.26** Muscles of the lateral right thigh.

**TABLE 8.12 Muscles of the Pelvic Floor**

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Levator ani | Pubis and ischial spine | Coccyx | Supports pelvic viscera, compresses anal canal |
| Coccygeus | Ischial spine | Sacrum and coccyx | Supports pelvic viscera, compresses anal canal |
| Superficial transversus perinei | Ischial tuberosity | Central tendon | Supports pelvic viscera |
| Bulbospongiosus | Central tendon | Males: Corpus cavernosa of penis<br>Females: Corpus cavernosa of clitoris | Males: Assists emptying of urethra, assists erection of penis<br>Females: Constricts vagina, assists erection of clitoris |
| Ischiocavernosus | Ischial tuberosity | Corpus cavernosa of penis or clitoris | Helps maintain erection of penis or clitoris |

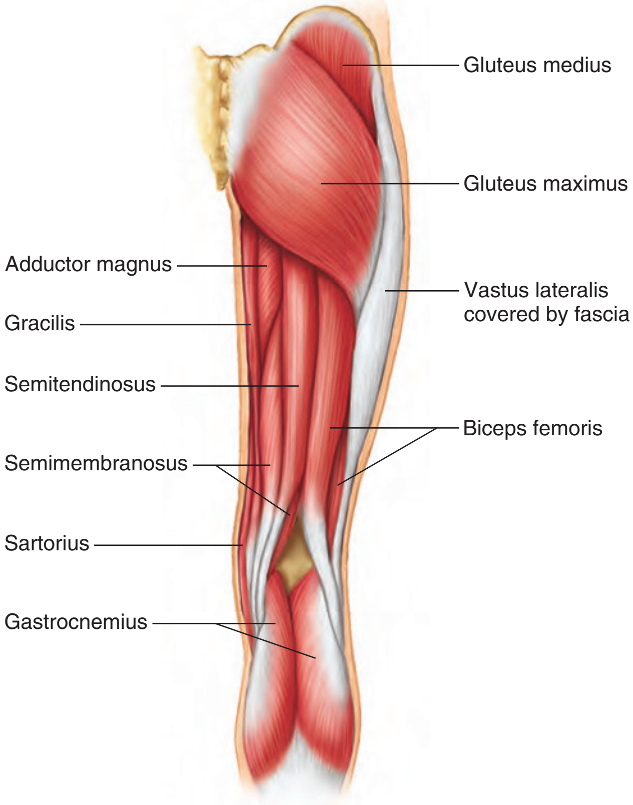


**FIGURE 8.27** APR Muscles of the posterior right thigh.

**Anterior group**
*psoas major* (so′as)
*iliacus* (il′e-ak-us)

**Posterior group**
*gluteus maximus* (gloo′te-us mak′si-mus)
*gluteus medius* (gloo′te-us me′de-us)
*gluteus minimus* (gloo′te-us min′ĭ-mus)
*tensor fasciae latae* (ten′sor fash′e-e lah-tē)

Still another group of muscles attached to the femur and pelvic girdle adduct the thigh. They include (figs. 8.25 and 8.27):

*adductor longus* (ah-duk′tor long′gus)
*adductor magnus* (ah-duk′tor mag′nus)
*gracilis* (gras′il-is)

Table 8.13 lists the origins, insertions, and actions of muscles that move the thigh.

## Muscles That Move the Leg

Muscles that move the leg connect the tibia or fibula to the femur or to the pelvic girdle. They can be separated into two major groups—those that flex the knee and those that extend the knee. Muscles of these groups include the hamstring group and the quadriceps femoris group (figs. 8.25, 8.26, and 8.27):

**Flexors**
*biceps femoris* (bi′seps fem′or-is)
*semitendinosus* (sem″e-ten′dĭ-no-sus)
*semimembranosus* (sem″e-mem′brah-no-sus)
*sartorius* (sar-to′re-us)

**Extensor**
*quadriceps femoris group* (kwod′rĭ-seps fem′or-is)
Composed of four parts—the rectus femoris, vastus lateralis, vastus medialis, and vastus intermedius.

Table 8.14 lists the origins, insertions, and actions of muscles that move the leg.

## Muscles That Move the Foot

A number of muscles that move the foot are in the leg. They attach the femur, tibia, and fibula to bones of the foot, move the foot upward (dorsiflexion) or downward (plantar flexion), and turn the sole of the foot medial

**TABLE 8.13** Muscles That Move the Thigh APR

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Psoas major | Bodies and transverse processes of lumbar vertebrae | Lesser trochanter of femur | Flexes thigh at hip |
| Iliacus | Iliac fossa of ilium | Lesser trochanter of femur | Flexes thigh at hip |
| Gluteus maximus | Sacrum, coccyx, and posterior surface of ilium | Posterior surface of femur and fascia of thigh | Extends thigh at hip |
| Gluteus medius | Lateral surface of ilium | Greater trochanter of femur | Abducts thigh, rotates thigh medially |
| Gluteus minimus | Lateral surface of ilium | Greater trochanter of femur | Abducts thigh, rotates thigh medially |
| Tensor fasciae latae | Anterior iliac crest | Fascia of thigh | Abducts thigh, rotates thigh medially |
| Adductor longus | Pubic bone near pubic symphysis | Posterior surface of femur | Adducts thigh, flexes thigh at hip |
| Adductor magnus | Ischial tuberosity | Posterior surface of femur | Adducts thigh, extends thigh at hip |
| Gracilis | Lower edge of pubic symphysis | Proximal medial surface of tibia | Adducts thigh, flexes thigh at hip, rotates lower limb medially |

## TABLE 8.14 Muscles That Move the Leg

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Sartorius | Anterior superior iliac spine | Medial surface of tibia | Flexes leg at knee, flexes thigh at hip, abducts thigh, rotates thigh laterally, rotates leg medially |
| Hamstring group | | | |
| Biceps femoris | Ischial tuberosity and posterior surface of femur | Head of fibula | Flexes leg at knee, extends thigh at hip |
| Semitendinosus | Ischial tuberosity | Proximal medial surface of tibia | Flexes leg at knee, extends thigh at hip |
| Semimembranosus | Ischial tuberosity | Medial condyle of tibia | Flexes leg at knee, extends thigh at hip |
| Quadriceps femoris group | | | |
| Rectus femoris | Anterior inferior iliac spine and margin of acetabulum | Patella, by the tendon which continues as patellar ligament to tibial tuberosity | Extends leg at knee, flexes thigh at hip |
| Vastus lateralis | Greater trochanter and posterior surface of femur | Patella, by the tendon which continues as patellar ligament to tibial tuberosity | Extends leg at knee |
| Vastus medialis | Medial surface of femur | Patella, by the tendon which continues as patellar ligament to tibial tuberosity | Extends leg at knee |
| Vastus intermedius | Anterior and lateral surfaces of femur | Patella, by the tendon which continues as patellar ligament to tibial tuberosity | Extends leg at knee |

(inversion) or lateral (eversion). These muscles include (figs. 8.28, 8.29, and 8.30):

**Dorsiflexors**
*tibialis anterior* (tib″e-a′lis an-te′re-or)
*fibularis (peroneus) tertius* (fib″u-la′ris ter′shus)
*extensor digitorum longus* (eks-ten′sor dij″ĭ-to′rum long′gus)

**Plantar flexors**
*gastrocnemius* (gas″trok-ne′me-us)
*soleus* (so′le-us)
*flexor digitorum longus* (flek′sor dij″ĭ-to′rum long′gus)

**Invertor**
*tibialis posterior* (tib″e-a′lis pos-tēr′e-or)

**Evertor**
*fibularis (peroneus) longus* (fib″u-la′ris long′gus)

Table 8.15 lists the origins, insertions, and actions of muscles that move the foot.

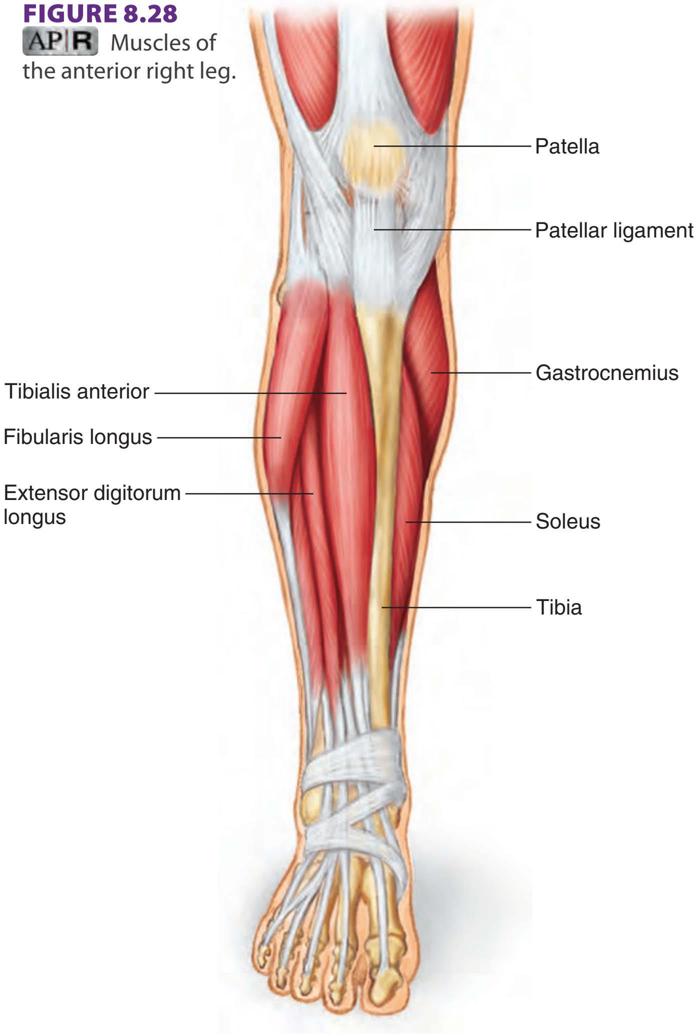


**FIGURE 8.28** Muscles of the anterior right leg.

## PRACTICE

29. What information is imparted in a muscle's name?
30. Which muscles provide facial expressions? ability to chew? head movements?
31. Which muscles move the pectoral girdle? abdominal wall? pelvic outlet? the arm, forearm, and hand? the thigh, leg, and foot?

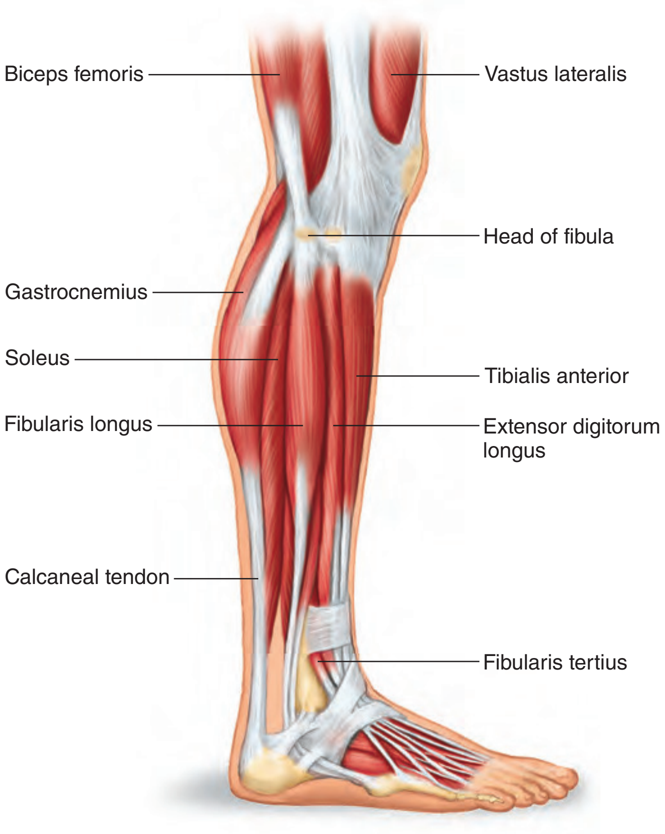

Biceps femoris
Vastus lateralis
Head of fibula
Gastrocnemius
Soleus
Tibialis anterior
Fibularis longus
Extensor digitorum longus
Calcaneal tendon
Fibularis tertius

**FIGURE 8.29** Muscles of the lateral right leg. (Note that the tibialis posterior is a deep muscle not visible in this view.)

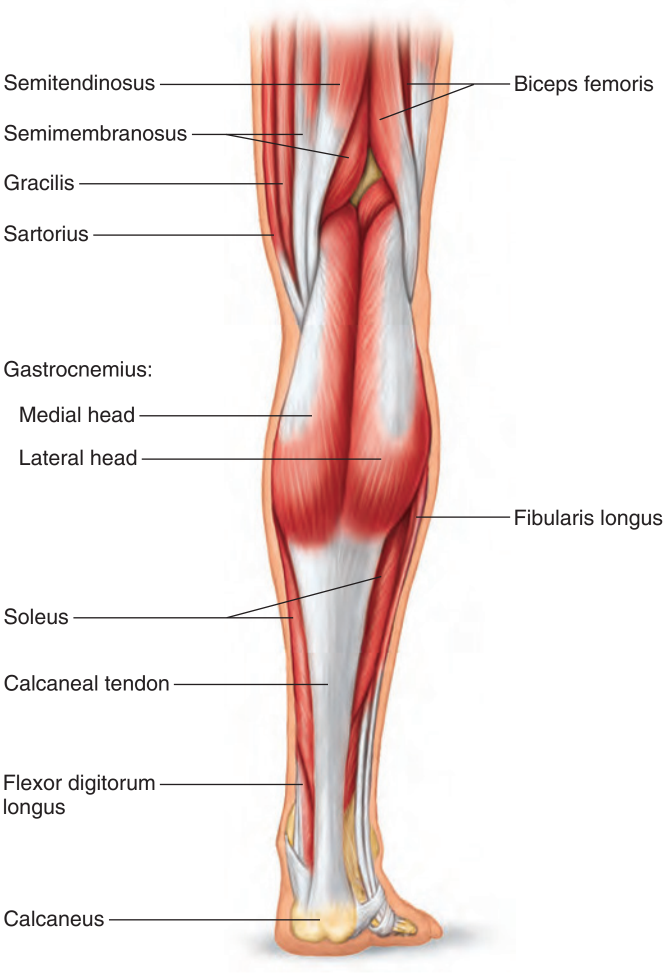
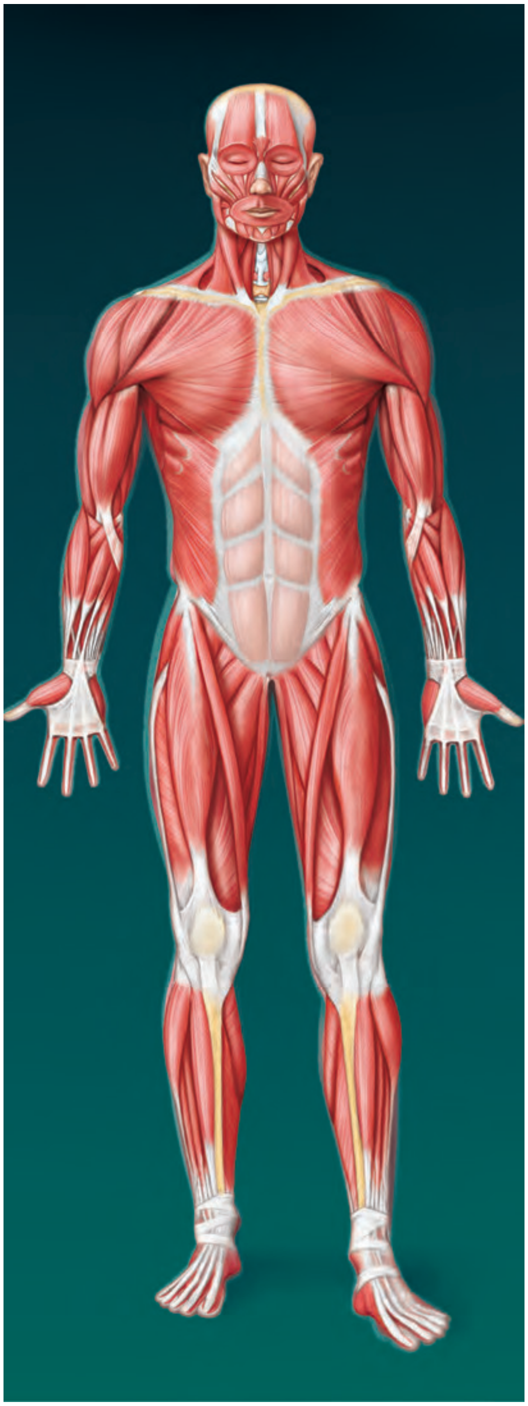

Semitendinosus
Biceps femoris
Semimembranosus
Gracilis
Sartorius
Gastrocnemius:
Medial head
Lateral head
Fibularis longus
Soleus
Calcaneal tendon
Flexor digitorum longus
Calcaneus

**FIGURE 8.30** APR Muscles of the posterior right leg.

**TABLE 8.15** **Muscles That Move the Foot** APR

| Muscle | Origin | Insertion | Action |
|---|---|---|---|
| Tibialis anterior | Lateral condyle and lateral surface of tibia | Tarsal bone (medial cuneiform) and first metatarsal | Dorsiflexion and inversion of foot |
| Fibularis tertius | Anterior surface of fibula | Dorsal surface of fifth metatarsal | Dorsiflexion and eversion of foot |
| Extensor digitorum longus | Lateral condyle of tibia and anterior surface of fibula | Dorsal surfaces of middle and distal phalanges of the four lateral toes | Dorsiflexion of foot, extension of toes |
| Gastrocnemius | Lateral and medial condyles of femur | Posterior surface of calcaneus | Plantar flexion of foot, flexion of leg at knee |
| Soleus | Head and shaft of fibula and posterior surface of tibia | Posterior surface of calcaneus | Plantar flexion of foot |
| Flexor digitorum longus | Posterior surface of tibia | Distal phalanges of the four lateral toes | Plantar flexion and inversion of foot, flexion of the four lateral toes |
| Tibialis posterior | Lateral condyle and posterior surface of tibia, and posterior surface of fibula | Tarsal and metatarsal bones | Plantar flexion and inversion of foot |
| Fibularis longus | Lateral condyle of tibia and head and shaft of fibula | Tarsal bone (medial cuneiform) and first metatarsal | Plantar flexion and eversion of foot; also supports arch |

# Muscular System



Muscles provide the force for moving body parts.

## Integumentary System

The skin increases heat loss during skeletal muscle activity.

## Skeletal System

Bones provide attachments that allow skeletal muscles to cause movement.

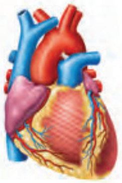
## Nervous System

Neurons control muscle contractions.

## Endocrine System

Hormones help increase blood flow to exercising skeletal muscles.

## Cardiovascular System



The heart pumps as a result of cardiac muscle contraction. Blood flow delivers oxygen and nutrients and removes wastes.

## Lymphatic System

Muscle action pumps lymph through lymphatic vessels.

## Digestive System

Skeletal muscles are important in swallowing. The digestive system absorbs nutrients needed for muscle contraction.

## Respiratory System

Breathing depends on skeletal muscles. The lungs provide oxygen for body cells and excrete carbon dioxide.

## Urinary System

Skeletal muscles help control expulsion of urine from the urinary bladder.

## Reproductive System

Skeletal muscles are important in sexual activity.

## Summary Outline

### 8.1 Introduction (p. 189)

*The three types of muscle tissue are skeletal, smooth, and cardiac.*

### 8.2 Structure of a Skeletal Muscle (p. 189)

*Individual muscles are the organs of the muscular system. They include skeletal muscle tissue, nervous tissue, blood, and connective tissues.*

1. Connective tissue coverings
   a. Fascia covers skeletal muscles.
   b. Other connective tissues attach muscles to bones or to other muscles.
   c. A network of connective tissue extends throughout the muscular system.
2. Skeletal muscle fibers
   a. Each skeletal muscle fiber is a single muscle cell.
   b. The cytoplasm contains mitochondria, sarcoplasmic reticulum, and myofibrils of actin and myosin.
   c. The organization of actin and myosin filaments produces striations.
   d. Transverse tubules extend inward from the cell membrane and associate with the sarcoplasmic reticulum.
3. Neuromuscular junction
   a. Motor neurons stimulate muscle fibers to contract.
   b. In response to an impulse, the end of a motor neuron axon secretes a neurotransmitter, which stimulates the muscle fiber to contract.

### 8.3 Skeletal Muscle Contraction (p. 193)

*Muscle fiber contraction results from a sliding movement of actin and myosin filaments.*

1. Role of myosin and actin
   a. Heads of myosin filaments form cross-bridge linkages with actin filaments.
   b. The reaction between actin and myosin filaments generates the force of contraction.
2. Stimulus for contraction
   a. Acetylcholine released from the distal end of a motor neuron axon stimulates a skeletal muscle fiber.
   b. Acetylcholine causes the muscle fiber to conduct an impulse over the surface of the fiber that reaches deep within the fiber through the transverse tubules.
   c. The impulse signals the sarcoplasmic reticulum to release calcium ions.
   d. Cross-bridge linkages form between actin and myosin, and the cross-bridges pull on actin filaments, shortening the fiber.
   e. The muscle fiber relaxes when myosin heads release from actin, breaking the cross-bridges (ATP is needed, but is not broken down) and when calcium ions are actively transported (requiring ATP breakdown) back into the sarcoplasmic reticulum.
   f. Acetylcholinesterase breaks down acetylcholine.
3. Energy sources for contraction
   a. ATP supplies the energy for muscle fiber contraction.
   b. Creatine phosphate stores energy that can be used to synthesize ATP.
   c. ATP is needed for muscle relaxation.
4. Oxygen supply and cellular respiration
   a. Aerobic respiration requires oxygen.
   b. Red blood cells carry oxygen to body cells.
   c. Myoglobin in muscle cells helps maintain oxygen availability.
5. Oxygen debt
   a. During rest or moderate exercise, muscles receive enough oxygen to respire aerobically.
   b. During strenuous exercise, oxygen deficiency may cause lactic acid to be produced. Lactic acid dissociates to form lactate.
   c. Oxygen debt is the amount of oxygen required to convert lactate to glucose and to restore supplies of ATP and creatine phosphate.
6. Muscle fatigue
   a. A fatigued muscle loses its ability to contract.
   b. Muscle fatigue may be due in part to increased production of lactic acid.
7. Heat production
   a. More than half of the energy released in cellular respiration is lost as heat.
   b. Muscle action is an important source of body heat.

### 8.4 Muscular Responses (p. 198)

1. Threshold stimulus is the minimal stimulus required to elicit a muscular contraction.
2. Recording a muscle contraction
   a. A twitch is a single, short contraction reflecting stimulation of a muscle fiber.
   b. A myogram is a recording of an electrically stimulated isolated muscle.
   c. The latent period, the time between stimulus and responding muscle contraction, is followed by a period of contraction and a period of relaxation.
3. Summation
   a. A rapid series of stimuli may produce summation of twitches.
   b. Very rapid stimulation can lead to partial or complete tetanic contraction.
4. Recruitment of motor units
   a. One motor neuron and the muscle fibers associated with it constitute a motor unit.
   b. All the muscle fibers of a motor unit contract together.
   c. Recruitment increases the number of motor units being activated in a whole muscle.
   d. The many motor units in a whole muscle are controlled by different motor neurons which respond to different thresholds of stimulation.
   e. At a low intensity of stimulation, small numbers of motor units contract.
   f. At increasing intensities of stimulation, other motor units are recruited until the muscle contracts with maximal force.
5. Sustained contractions
   a. Summation and recruitment together can produce a sustained contraction of increasing strength.
   b. Even when a muscle is at rest, its fibers usually remain partially contracted.

### 8.5 Smooth Muscle (p. 201)

*The contractile mechanism of smooth muscle is similar to that of skeletal muscle.*

1. Smooth muscle fibers
   a. Smooth muscle cells contain filaments of actin and myosin, less organized than those in skeletal muscle.
   b. Types include multiunit smooth muscle and visceral smooth muscle.
   c. Visceral smooth muscle displays rhythmicity and is self-exciting.

2. Smooth muscle contraction
    a. Two neurotransmitters—acetylcholine and norepinephrine—and hormones affect smooth muscle function.
    b. Smooth muscle can maintain a contraction longer with a given amount of energy than can skeletal muscle.
    c. Smooth muscles can change length without changing tension.

## 8.6 Cardiac Muscle (p. 201)

1. Like skeletal muscle cells, cardiac muscle cells have actin and myosin filaments that are well-organized and striated.
2. Cardiac muscle twitches last longer than skeletal muscle twitches.
3. Intercalated discs connect cardiac muscle cells.
4. A network of fibers contracts as a unit.
5. Cardiac muscle is self-exciting and rhythmic.

## 8.7 Skeletal Muscle Actions (p. 202)

*The type of movement a skeletal muscle produces depends on the way the muscle attaches on either side of a joint.*

1. Origin and insertion
    a. The relatively immovable end of a skeletal muscle is its origin, and the relatively movable end is its insertion.
    b. Some muscles have more than one origin.
2. Interaction of skeletal muscles
    a. Skeletal muscles function in groups.
    b. An agonist causes a movement.
    c. Antagonists are muscles that oppose a movement.
    d. Muscles that work together to assist a movement are synergists.
    e. An agonist doing most of the work to cause a movement is a prime mover.
    f. Smooth movements result from agonists and antagonists working together.

## 8.8 Major Skeletal Muscles (p. 204)

1. Muscles of facial expression
    a. These muscles lie beneath the skin of the face and scalp and are used to communicate feelings through facial expression.
    b. They include the epicranius, orbicularis oculi, orbicularis oris, buccinator, zygomaticus, and platysma.
2. Muscles of mastication
    a. These muscles attach to the mandible and are used in chewing.
    b. They include the masseter and temporalis.
3. Muscles that move the head
    a. Muscles in the neck and upper back move the head.
    b. They include the sternocleidomastoid, splenius capitis, semispinalis capitis, and the scalenes.
4. Muscles that move the pectoral girdle
    a. Most of these muscles connect the scapula to nearby bones and closely associate with muscles that move the arm.
    b. They include the trapezius, rhomboid major, levator scapulae, serratus anterior, and pectoralis minor.
5. Muscles that move the arm
    a. These muscles connect the humerus to various regions of the pectoral girdle, ribs, and vertebral column.
    b. They include the coracobrachialis, pectoralis major, teres major, latissimus dorsi, supraspinatus, deltoid, subscapularis, infraspinatus, and teres minor.
6. Muscles that move the forearm
    a. These muscles connect the radius and ulna to the humerus or pectoral girdle.
    b. They include the biceps brachii, brachialis, brachioradialis, triceps brachii, supinator, pronator teres, and pronator quadratus.
7. Muscles that move the hand
    a. These muscles arise from the distal end of the humerus and from the radius and ulna.
    b. They include the flexor carpi radialis, flexor carpi ulnaris, palmaris longus, flexor digitorum profundus, extensor carpi radialis longus, extensor carpi radialis brevis, extensor carpi ulnaris, and extensor digitorum.
8. Muscles of the abdominal wall
    a. These muscles connect the rib cage and vertebral column to the pelvic girdle.
    b. They include the external oblique, internal oblique, transversus abdominis, and rectus abdominis.
9. Muscles of the pelvic floor
    a. These muscles form the floor of the pelvic cavity and fill the space within the pubic arch.
    b. They include the levator ani, superficial transversus perinei, bulbospongiosus, and ischiocavernosus.
10. Muscles that move the thigh
    a. These muscles attach to the femur and to some part of the pelvic girdle.
    b. They include the psoas major, iliacus, gluteus maximus, gluteus medius, gluteus minimus, tensor fasciae latae, adductor longus, adductor magnus, and gracilis.
11. Muscles that move the leg
    a. These muscles connect the tibia or fibula to the femur or pelvic girdle.
    b. They include the biceps femoris, semitendinosus, semimembranosus, sartorius, and the quadriceps femoris group.
12. Muscles that move the foot
    a. These muscles attach the femur, tibia, and fibula to bones of the foot.
    b. They include the tibialis anterior, fibularis tertius, extensor digitorum longus, gastrocnemius, soleus, flexor digitorum longus, tibialis posterior, and fibularis longus.

# CHAPTER ASSESSMENTS

## 8.1 Introduction

**1.** The three types of muscle tissue are __________, __________, and __________. (p. 189)

## 8.2 Structure of a Skeletal Muscle

**2.** Describe the difference between a tendon and an aponeurosis. (p. 189)

**3.** Describe how connective tissue associates with skeletal muscle. (pp. 189–190)

**4.** List the major parts of a skeletal muscle fiber, and describe the function of each part. (p. 190)

**5.** Describe a neuromuscular junction. (p. 192)

**6.** A neurotransmitter __________. (p. 192)

a. binds actin filaments, causing them to slide
b. diffuses across a synapse from a neuron to a muscle cell
c. carries ATP across a synapse
d. travels across a synapse from a muscle cell to a neuron

## 8.3 Skeletal Muscle Contraction

**7.** List the major events of muscle fiber contraction and relaxation. (p. 193)

**8.** Describe how ATP and creatine phosphate interact. (p. 195)

**9.** Describe how muscles obtain oxygen. (p. 196)

**10.** Describe how an oxygen debt may develop. (p. 196)

**11.** Explain how muscles may become fatigued. (p. 197)

**12.** Explain how skeletal muscle function affects the maintenance of body temperature. (p. 197)

## 8.4 Muscular Responses

**13.** Define *threshold stimulus.* (p. 198)

**14.** Sketch a myogram of a single muscular twitch, and identify the latent period, period of contraction, and period of relaxation. (p. 198)

**15.** Define *motor unit.* (p. 199)

**16.** Which of the following describes the addition of muscle fibers to take part in a contraction? (p. 199)

a. summation
b. recruitment
c. tetany
d. twitch

**17.** Explain how skeletal muscle stimulation produces a sustained contraction. (p. 200)

**18.** Distinguish between tetanic contraction and muscle tone. (pp. 199–200)

## 8.5 Smooth Muscle

**19.** Distinguish between multiunit and visceral smooth muscle fibers. (p. 201)

**20.** Compare smooth and skeletal muscle contractions. (p. 201)

## 8.6 Cardiac Muscle

**21.** Make a table comparing contraction mechanisms of cardiac and skeletal muscle fibers. (p. 202)

## 8.7 Skeletal Muscle Actions

**22.** Distinguish between a muscle's origin and its insertion. (p. 202)

**23.** Define *agonist, antagonist,* and *synergist.* (p. 204)

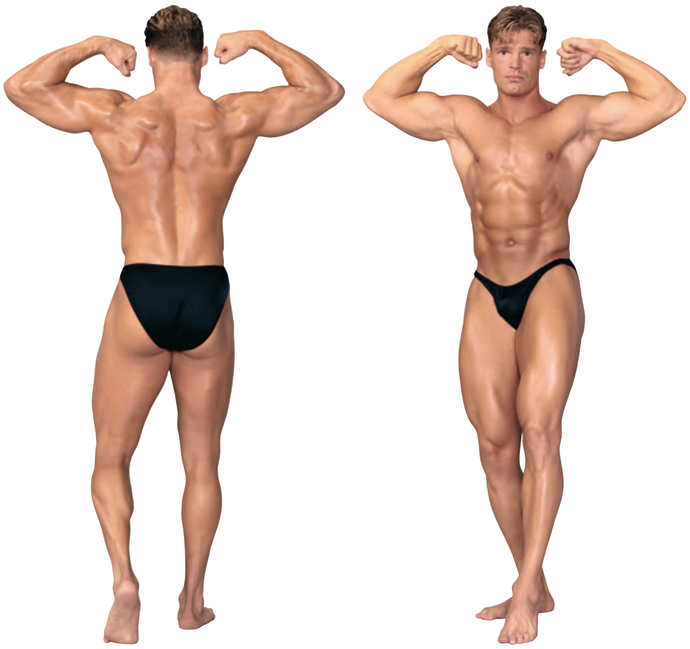
## 8.8 Major Skeletal Muscles

**24.** Match the muscles to their descriptions and functions. (pp. 204–217)

(1) buccinator
(2) epicranius
(3) orbicularis oris
(4) platysma
(5) rhomboid major
(6) splenius capitis
(7) temporalis
(8) zygomaticus
(9) biceps brachii
(10) brachialis
(11) deltoid
(12) latissimus dorsi
(13) pectoralis major
(14) pronator teres
(15) teres minor
(16) triceps brachii
(17) biceps femoris
(18) external oblique
(19) gastrocnemius
(20) gluteus maximus
(21) gluteus medius
(22) gracilis
(23) rectus femoris
(24) tibialis anterior

A. inserted on coronoid process of mandible
B. elevates corner of mouth
C. elevates scapula
D. brings head into an upright position
E. elevates eyebrow
F. compresses cheeks
G. fascia in upper chest is origin
H. closes lips
I. extends forearm at elbow
J. extends arm at shoulder
K. abducts arm
L. inserted on radial tuberosity
M. flexes arm at shoulder
N. pronates forearm
O. inserted on coronoid process of ulna
P. rotates arm laterally
Q. inverts foot
R. member of quadriceps femoris group
S. plantar flexor of foot
T. compresses contents of abdominal cavity
U. extends thigh at hip
V. hamstring muscle
W. adducts thigh
X. abducts thigh

**25.** Which muscles can you identify in the bodies of these models? (pp. 204–217)



## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 4.4, 8.3

1. As lactate and other substances accumulate in an active muscle, they stimulate pain receptors and the muscle may feel sore. How might the application of heat or substances that dilate blood vessels relieve such soreness?

### OUTCOMES 5.3, 8.2

2. Discuss how connective tissue is part of the muscular system.

### OUTCOMES 8.3, 8.4

3. A woman takes her daughter to a sports medicine specialist and requests that the specialist determine the percentage of fast- and slow-twitch fibers in the girl's leg muscles. The parent wants to know if the healthy girl should try out for soccer or cross-country running. Do you think this is a valid reason to test muscle tissue? Why or why not?

4. Following an injury to a nerve, the muscle it supplies with motor nerve fibers may become paralyzed. How would you explain to a patient the importance of moving the disabled muscles passively or contracting them using electrical stimulation?

### OUTCOMES 8.4, 8.8

5. What steps might be taken to minimize atrophy of the skeletal muscles in patients confined to bed for prolonged times?

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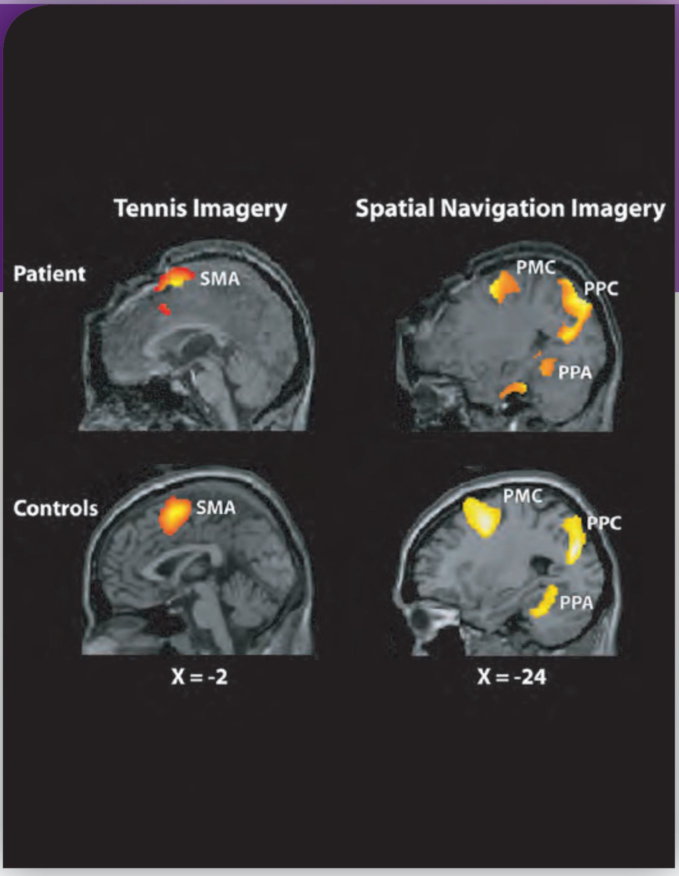
# 9

# Nervous System



*A woman who had suffered brain injury in a traffic accident and was in a persistent vegetative state was asked to imagine herself playing tennis and walking through the rooms of her home, while undergoing neuroimaging with functional MRI. Although she could not move or respond verbally, the patterns in which her brain lit up matched those of 12 healthy individuals as they completed the same tasks.*

"Islands of awareness" in the vegetative brain. The twenty-three-year-old had been in a persistent vegetative state for five months after sustaining traumatic brain injury in a car accident. She was awake, but apparently not aware, and unable to communicate in any way. To an observer, she had no sense of her own existence and did not react to sight or sound. But the young woman was aware—she just could not communicate.

British researchers used functional MRI (fMRI), a form of neuroimaging that measures regional blood flow, to give the patient a way to communicate in response to a stimulus. In a preliminary experiment, fMRI tracked her response to speech. First she heard a sentence that made sense, and then a sentence that had the same cadence as the first but was all nonsense words. Her brain lit up in the speech-processing centers only when the sentence she heard had meaning. When she heard a sentence that included a homonym—a word that could have either of two meanings—an additional brain region lit up.

The researchers next asked the patient to imagine herself playing tennis and then walking through her house. Healthy individuals asked to do the same were controls. The young woman's brain and the control brains lit up in exactly the same areas. The researchers then devised a new set of experiments in which people in vegetative states who responded to "tennis" and "house" were told to use these imaginings as stand-ins for the words "yes" and "no." The test was to then ask the patients yes-no questions, and have them answer by imagining either being in a house or playing tennis; one image meant "yes" and one meant "no." The questions were highly specific about their pasts. When the patients imagined "tennis" or "house," the results were seen in the fMRI. They were correct every time, even after researchers switched the meanings from "tennis" signifying no and "house" yes to the opposite. This discovery of what the researchers call "islands of awareness" in the brain is changing the way that we view a persistent vegetative state. However, not all patients respond this way.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 9.1 Introduction

1. Distinguish between the two types of cells that compose nervous tissue. (p. 224)
2. Name the two major groups of nervous system organs. (p. 225)

### 9.2 General Functions of the Nervous System

3. Explain the general functions of the nervous system. (p. 225)

### 9.3 Neuroglia

4. State the functions of neuroglia in the central nervous system. (p. 226)
5. Distinguish among the types of neuroglia in the central nervous system. (p. 226)
6. Describe the Schwann cells of the peripheral nervous system. (p. 227)

### 9.4 Neurons

7. Describe the general structure of a neuron. (p. 228)
8. Explain how differences in structure and function are used to classify neurons. (pp. 228–231)

### 9.5 The Synapse

9. Explain how information passes from one neuron to another. (p. 232)

### 9.6 Cell Membrane Potential

10. Explain how a membrane becomes polarized. (p. 232)
11. Describe the events that lead to the generation of an action potential. (p. 236)

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**Module 7**
Nervous System

### 9.7 Impulse Conduction

12. Compare impulse conduction in myelinated and unmyelinated neurons. (p. 236)

### 9.8 Synaptic Transmission

13. Identify the changes in membrane potential associated with excitatory and inhibitory neurotransmitters. (p. 239)

### 9.9 Impulse Processing

14. Describe the general ways in which the nervous system processes information. (p. 240)

### 9.10 Types of Nerves

15. Describe how nerves are classified. (p. 241)

### 9.11 Nerve Pathways

16. Describe the function of each part of a reflex arc, and name two reflex examples. (p. 242)

### 9.12 Meninges

17. Describe the coverings of the brain and spinal cord. (p. 243)

### 9.13 Spinal Cord

18. Describe the structure of the spinal cord and its major functions. (p. 245)

### 9.14 Brain

19. Name the major parts and functions of the brain. (pp. 247–257)
20. Distinguish among sensory, association, and motor areas of the cerebral cortex. (p. 250)
21. Describe the location, formation, and function of cerebrospinal fluid. (p. 252)

### 9.15 Peripheral Nervous System

22. List the major parts of the peripheral nervous system. (pp. 257–258)
23. Name the cranial nerves, and list their major functions. (pp. 258–260)
24. Describe the structure of a spinal nerve. (p. 261)

### 9.16 Autonomic Nervous System

25. Describe the functions of the autonomic nervous system. (p. 262)
26. Distinguish between the sympathetic and parasympathetic divisions of the autonomic nervous system. (p. 262)
27. Describe a sympathetic and a parasympathetic nerve pathway. (pp. 263–265)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**ax-** [axis] *ax*on: Cylindrical nerve fiber that carries impulses away from a neuron cell body.

**dendr-** [tree] *dendr*ite: Branched nerve cell process that serves as a receptor surface of a neuron.

**funi-** [small cord or fiber] *funi*culus: Major nerve tract or bundle of myelinated nerve cell axons in the spinal cord.

**gangli-** [a swelling] *gangli*on: Mass of neuron cell bodies.

**-lemm** [rind or peel] neuri*lemm*a: Sheath that surrounds the myelin of a nerve cell axon.

**mening-** [membrane] *mening*es: Membranous coverings of the brain and spinal cord.

**moto-** [moving] *motor* neuron: Neuron that stimulates a muscle to contract or a gland to secrete.

**peri-** [around] *peri*pheral nervous system: Portion of the nervous system that consists of nerves branching from the brain and spinal cord.

**plex-** [interweaving] choroid *plex*us: Mass of specialized capillaries associated with spaces in the brain.

**sens-** [feeling] *sens*ory neuron: Neuron that conducts impulses into the brain or spinal cord.

**syn-** [together] *syn*apse: Junction between two neurons.

**ventr-** [belly or stomach] *ventr*icle: Fluid-filled space in the brain.

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## 9.1 | Introduction

Feeling, thinking, remembering, moving, and being aware of the world require activity from the nervous system. This vast collection of cells also helps coordinate all other body functions to maintain homeostasis and to enable the body to respond to changing conditions. Information from inside and outside the body is brought to the brain and spinal cord, which then stimulate responses from muscles and glands.

Recall from chapter 5 (p. 122) that nervous tissue consists of masses of nerve cells, or **neurons.** These cells are the main functional units of the nervous system and are specialized to react to physical and chemical changes in their surroundings (fig. 9.1). Neurons carry information in the form of electrochemical changes, called **impulses,** which allow them to communicate with other neurons and with cells outside the nervous system.

The impulse conducted along an axon is often referred to as a nerve impulse. This may be misleading, because the term "nerve" in anatomy refers to a bundle of axons, not an individual cell. A similar situation arises when referring to a neuron as a nerve cell. We continue to use both of the terms "nerve impulse" "and nerve cell" in this book because they are familiar to teachers and students, but we feel it is important to point out this departure from strict anatomical terminology.

A typical neuron has a rounded area called the **cell body,** and two types of extensions: dendrites and axons. **Dendrites,** which may be numerous, receive input, and **axons** send information away from the cell in the form of impulses. Most neurons have only one axon. Figure 9.1 depicts these major parts of a neuron.

Nervous tissue also includes **neuroglia** that provide physical support, insulation, and nutrients for neurons.

During development before birth, neuroglia release and relay signals that guide the differentiation of neurons from progenitor cells (see chapter 3, p. 82).

An important part of the nervous system at the cellular level is not a cell at all, but the small space between a neuron and the cell(s) with which it communicates, called a **synapse** (sin′aps). Biological messenger molecules called **neurotransmitters** (nu″ro-trans-mit′erz) convey neural information across synapses.

The organs of the nervous system can be divided into two groups. One group, consisting of the brain and spinal cord, forms the **central nervous system (CNS).** The other, composed of the nerves (bundles of axons) that connect the central nervous system to other body parts, is called the **peripheral nervous system (PNS)** (fig. 9.2). Together, these systems provide three general functions: sensory, integrative, and motor.

**PRACTICE**

1. What are the two major types of cells that form nervous tissue?
2. What are the two major subdivisions of the nervous system?

## 9.2 General Functions of the Nervous System

The *sensory function* of the nervous system derives from **sensory receptors** (sen′so-re re-sep′torz) at the ends of peripheral neurons (see chapter 10, p. 274). These receptors gather information by detecting changes inside and outside the body. Sensory receptors monitor external environmental factors, such as light and sound intensities, and conditions of the body's internal environment, such as temperature and oxygen level.

Sensory receptors convert environmental information into impulses, which are then conducted on peripheral nerves to the central nervous system. There, the signals are integrated; that is, they are brought together, creating sensations, adding to memory, or helping produce thoughts that translate sensations into perceptions. As a result of this *integrative function,* we make conscious or subconscious decisions, and then we use *motor functions* to act on them.

The motor functions of the nervous system employ peripheral neurons, which conduct impulses from the central nervous system to responsive structures called **effectors** (e-fek′torz). Effectors, which are outside the nervous system, include muscles and glands whose actions are either controlled or modified by neurons.

The motor functions of the peripheral nervous system can be divided into two categories. Those that are under voluntary (conscious) control compose the **somatic nervous system,** which controls skeletal muscle. In contrast, the **autonomic nervous system**

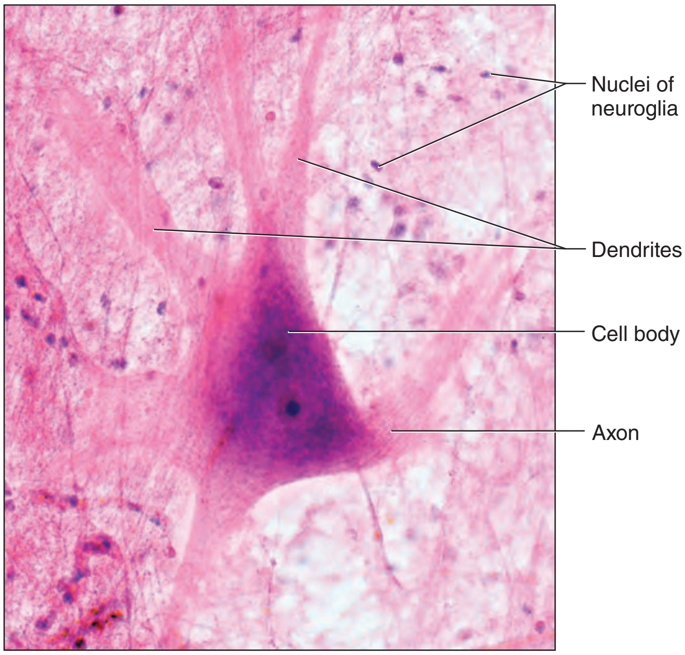


**FIGURE 9.1** APR Neurons are the structural and functional units of the nervous system (600×). The dark spots in the area surrounding the neuron are the nuclei of neuroglia. Note the dendrites and the single axon of the neuron.

CAREER CORNER

### Occupational Therapist

The man with amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease) had been growing frustrated with his increasing inability to carry out the activities of daily living. He couldn't use his hands, and his wrists were growing weaker. A visit from an occupational therapist greatly improved both his independence and his spirit.

The occupational therapist showed the man how to continue to use a bathroom sink by supporting his weight on his arms, and how to use mirrors to compensate for his neck stiffness. The therapist was comforting and practical as he demonstrated how to repurpose metal salad tongs to hold toilet paper to care for bathroom needs.

An occupational therapist helps a person maintain normal activities while struggling with a disease, injury, disability, or other limitation. The therapist evaluates the patient's situation and how it is likely to change, sets goals, researches and presents interventions and adaptive equipment that may help, and assesses results. The therapist may also instruct family members and caregivers on how to assist the patient.

Occupational therapists work in health-care facilities, schools, home health services, and nursing homes. They must have a master's degree in occupational therapy and state licensure.

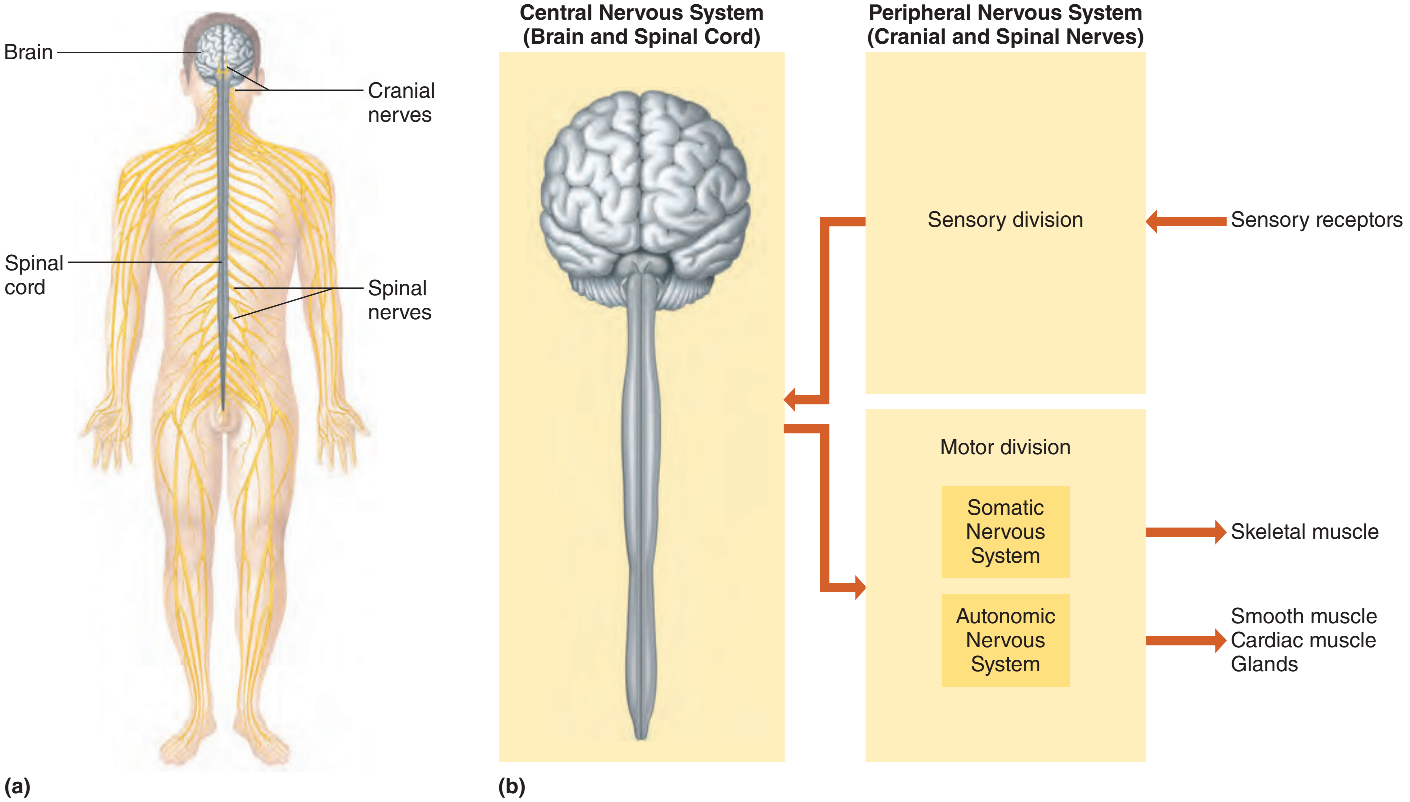

Brain
Cranial nerves
Spinal cord
Spinal nerves
(a)
Central Nervous System (Brain and Spinal Cord)
Peripheral Nervous System (Cranial and Spinal Nerves)
Sensory division
Sensory receptors
Motor division
Somatic Nervous System
Skeletal muscle
Autonomic Nervous System
Smooth muscle
Cardiac muscle
Glands
(b)

**FIGURE 9.2** Nervous system. **(a)** The nervous system includes the central nervous system (brain and spinal cord) and the peripheral nervous system (cranial nerves and spinal nerves). **(b)** The nervous system receives information from sensory receptors and initiates responses through effector organs (muscles and glands).

controls effectors that are involuntary, such as cardiac muscle, smooth muscle, and various glands.

The nervous system can detect changes outside and inside the body, make decisions based on the information received, and stimulate muscles or glands to respond. Typically these responses counteract the effects of the changes detected, and in this way the nervous system helps maintain homeostasis.

**PRACTICE**

3. How do sensory receptors collect information?
4. How does the central nervous system integrate incoming information?
5. What are the two types of motor functions of the nervous system?

## 9.3 | Neuroglia

Neurons cannot exist without neuroglia, which fill spaces, provide structural frameworks, produce the components of the electrical insulator **myelin** (mi′ĕ-lin), and carry on phagocytosis. In the central nervous system, neuroglia greatly outnumber neurons, and can divide, whereas neurons do not normally divide. Neuroglia in the central nervous system are of the following types (fig. 9.3):

1. **Microglial cells** are scattered throughout the central nervous system. They support neurons and phagocytize bacterial cells and cellular debris, and form scars in areas of damage.
2. **Oligodendrocytes** align along axons (nerve fibers). They provide insulating layers of myelin, called a **myelin sheath** (mi′ĕ-lin shēth) around axons within the brain and spinal cord.
3. **Astrocytes,** commonly found between neurons and blood vessels, provide structural support, join parts by their abundant cellular processes, and help regulate the concentrations of nutrients and ions within the tissue. Astrocytes also form scar tissue that fills spaces following injury to the CNS.
4. **Ependymal cells** form an epithelial-like membrane that covers specialized brain parts (choroid plexuses) and form the inner linings that enclose spaces in the brain (ventricles) and spinal cord (central canal).

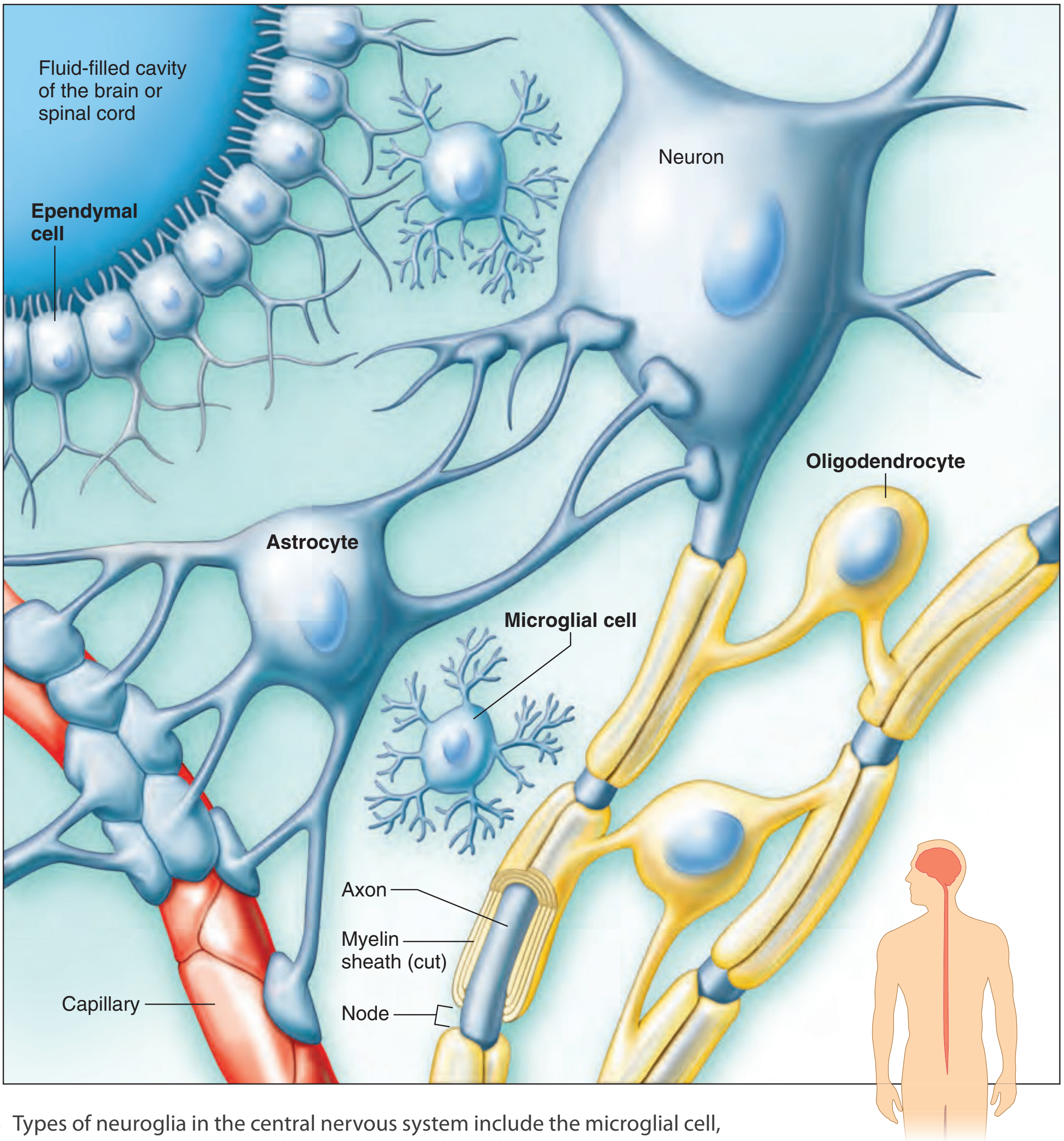


**FIGURE 9.3** Types of neuroglia in the central nervous system include the microglial cell, oligodendrocyte, astrocyte, and ependymal cell. (Ependymal cells have cilia into early childhood. In adults, cilia remain only on ependymal cells in the ventricles of the brain.)

Neuroglia assemble in a special, protective way in the brain. Most capillaries (the smallest blood vessels) are "leaky," allowing small molecules to enter or leave the bloodstream. The cells that form capillaries in the brain, in contrast, are much more tightly connected, thanks partly to astrocytes. This specialized architecture creates a "blood–brain barrier" that shields delicate brain tissue from chemical fluctuations, blocking entry to many substances. Drug developers must consider the barrier when formulating drugs that act in the brain, including ingredients that let the drug through.

The peripheral nervous system includes neuroglia called **Schwann cells.** They produce the myelin sheath around axons of myelinated neurons.

Too few and too many neuroglia can harm health. Fast-growing gliomas are brain tumors consisting of rapidly dividing neuroglia (neurons do not normally divide). Immediately after a spinal cord injury, destruction of neuroglia strips axons of myelin. Subsequent overgrowth of neuroglia forms scars, which impede recovery of function.

## PRACTICE

6. List the functions of the cells that support neurons.
7. Distinguish among the types of neuroglia in the central nervous system.
8. What is the function of Schwann cells in the peripheral nervous system?

# 9.4 | Neurons

## Neuron Structure

Neurons vary considerably in size and shape, but they all have common features. These include a cell body; the tubular, cytoplasm-filled dendrites, which conduct impulses to the neuron cell body; and an axon, which conducts impulses away from the neuron cell body.

The neuron cell body consists of granular cytoplasm, a cell membrane, and organelles such as mitochondria, lysosomes, a Golgi apparatus, and a network of fine threads called **neurofibrils** (nu″ro-fi′brilz), which extends into the axon. Scattered throughout the cytoplasm are many membranous sacs called **chromatophilic substance** (Nissl bodies). These are similar to rough endoplasmic reticulum in other cells (fig. 9.4). Ribosomes attached to chromatophilic substance function in protein synthesis, as they do elsewhere. Near the center of the cell body is a large, spherical nucleus with a conspicuous nucleolus.

Dendrites are usually short and highly branched. These processes, together with the membrane of the cell body, are the neuron's main receptive surfaces with which axons from other neurons communicate.

In most neurons the axon arises from the cell body as a cone-shaped thickening called the *axon hillock.* Many mitochondria, microtubules, and neurofibrils are in the axon cytoplasm. An axon originates as a single structure but may give off side branches (collaterals). Its end may branch into many fine extensions that contact the receptive surfaces of other cells.

Larger axons of peripheral neurons are enclosed in *myelin sheaths* produced by Schwann cells (figs. 9.4 and 9.5). These cells wind tightly around axons, somewhat like a bandage wrapped around a finger, coating them with many layers of cell membrane that have little or no cytoplasm between them. The parts of the Schwann cells that contain most of the cytoplasm and the nuclei remain outside the myelin sheath and compose a **neurilemma** (nu″rĭ-lem′ah), or neurilemmal sheath, which surrounds the myelin sheath. Narrow gaps between Schwann cells are called **nodes of Ranvier** (nō-dz uv ron′vee-ay) (fig. 9.5).

Axons with myelin sheaths are called *myelinated,* and those that lack sheaths are *unmyelinated.* Myelin is also in the CNS, where groups of myelinated axons appear white, and masses of such axons form the *white matter.* Unmyelinated axons and neuron cell bodies form *gray matter* in the CNS.

Myelin begins to form on axons during the fourteenth week of prenatal development. Yet many of the axons in newborns are not completely myelinated. As a result, an infant's nervous system cannot function as effectively as that of an older child or adult. Infants' responses to stimuli are coarse and undifferentiated, and may involve the whole body. All myelinated axons begin to develop sheaths by the time a child starts to walk, and myelination continues into adolescence. Deficiencies of essential nutrients during the developmental years may limit myelin formation, which may impair nervous system function later in life.

When peripheral nerves are damaged, their axons can regenerate. The neurilemma plays an important role in this process. In contrast, CNS axons are myelinated by oligodendrocytes, which do not provide a neurilemma. Consequently, damaged CNS neurons usually do not regenerate.

The brain harbors small collections of neural stem cells that can divide to give rise to new neurons or neuroglia, depending upon their chemical surroundings. Neural stem cells are found in the hippocampus and near the brain's ventricles.

**FACTS OF LIFE** To picture the relative sizes of a typical neuron's parts, imagine that the cell body is the size of a tennis ball. The axon would then be a mile long and half an inch thick. The dendrites would fill a large bedroom.

## Classification of Neurons

Neurons differ in the structure, size, and shape of their cell bodies. They also vary in the length and size of their axons and dendrites and in the number of connections they make with other neurons.

On the basis of structural differences, neurons are classified into three major groups (fig. 9.6). Each type of neuron is specialized to send an impulse in one direction.

1. **Multipolar neurons** have many processes arising from their cell bodies. Only one process of each neuron is an axon; the rest are dendrites. Most neurons whose cell bodies lie within the brain or spinal cord are multipolar.
2. **Bipolar neurons** have only two processes, one arising from each end of the cell body. These processes are structurally similar, but one is an axon and the other a dendrite. Neurons in specialized parts of the eyes, nose, and ears are bipolar.

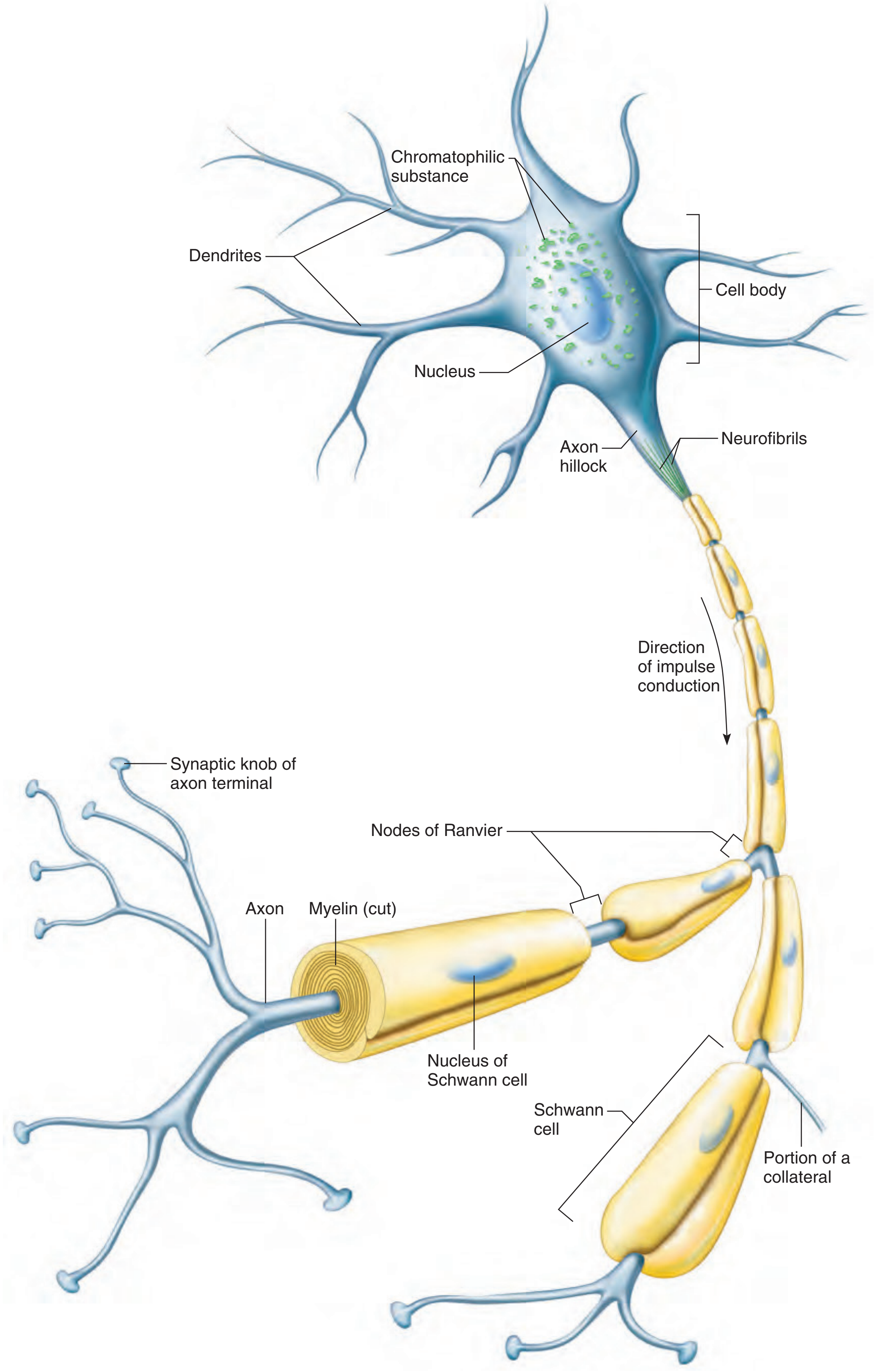

Chromatophilic substance
Dendrites
Cell body
Nucleus
Axon hillock
Neurofibrils
Direction of impulse conduction
Synaptic knob of axon terminal
Nodes of Ranvier
Axon
Myelin (cut)
Nucleus of Schwann cell
Schwann cell
Portion of a collateral

**FIGURE 9.4** A common neuron.

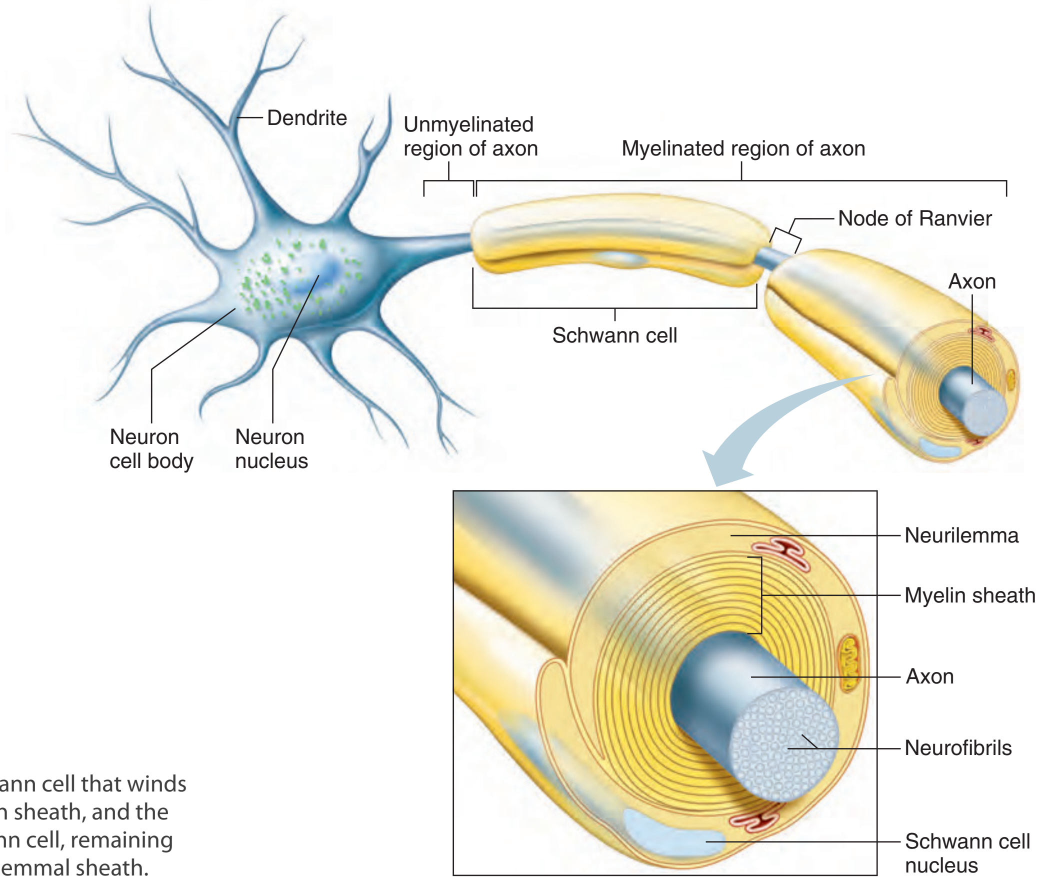
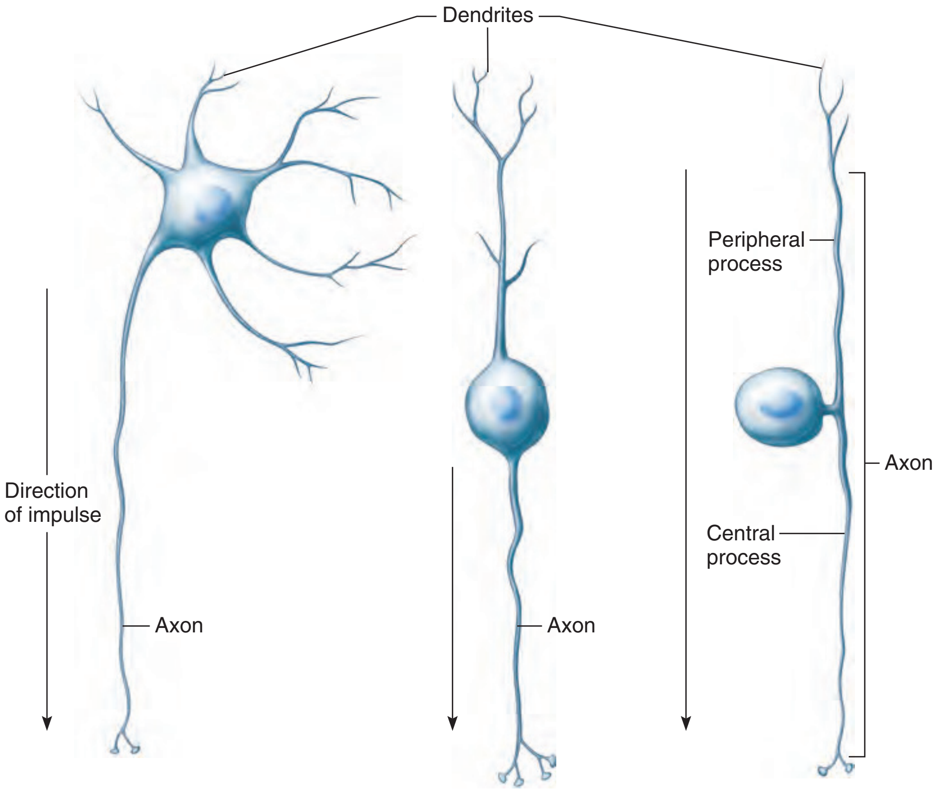

Dendrite
Unmyelinated region of axon
Myelinated region of axon
Node of Ranvier
Axon
Schwann cell
Neuron cell body
Neuron nucleus
Neurilemma
Myelin sheath
Axon
Neurofibrils
Schwann cell nucleus

**FIGURE 9.5** The portion of a Schwann cell that winds tightly around an axon forms a myelin sheath, and the cytoplasm and nucleus of the Schwann cell, remaining outside, form a neurilemma, or neurilemmal sheath.


Dendrites
Direction of impulse
Axon
Axon
Peripheral process
Central process
Axon

**(a)** Multipolar **(b)** Bipolar **(c)** Unipolar

**FIGURE 9.6** Structural types of neurons include **(a)** the multipolar neuron, **(b)** the bipolar neuron, and **(c)** the unipolar neuron.

3. **Unipolar neurons** have a single process extending from the cell body. A short distance from the cell body, this process divides into two branches, which really function as a single axon. One branch (the peripheral process) is associated with dendrites near a peripheral body part. The other branch (the central process) enters the brain or spinal cord. The cell bodies of unipolar neurons are found in some of the specialized masses of nervous tissue called **ganglia** (gang′gle-ah) (singular, *ganglion*), which are located outside the brain and spinal cord.

Neurons also vary in function. Different neurons may conduct impulses into the brain or spinal cord, conduct impulses from one area of the brain or spinal cord to another, or conduct impulses out of the brain or spinal cord. On the basis of functional differences, neurons are grouped as follows (fig. 9.7):

1. **Sensory neurons** (afferent neurons) conduct impulses from peripheral body parts into the brain or spinal cord. Sensory neurons either have specialized *receptor ends* at the tips of their dendrites, or they have dendrites that are closely associated with *receptor cells* in the skin or in sensory organs.

   Changes that occur inside or outside the body stimulate receptor ends or receptor cells, triggering sensory impulses. The impulses travel along the sensory neuron axons, which lead to the brain or spinal cord, where other neurons can process the impulses. Most sensory neurons are unipolar; some are bipolar.
2. **Interneurons** (also called *association* or *internuncial neurons*) lie entirely within the brain or spinal cord. They are multipolar and link other neurons. Interneurons conduct impulses from one part of the brain or spinal cord to another. That is, they may direct incoming sensory impulses to appropriate parts of the CNS for processing and interpreting. Other impulses are transferred to motor neurons. The cell bodies of some interneurons aggregate in specialized masses of nervous tissue called **nuclei** (singular, *nucleus*). Nuclei are similar to ganglia, but are within the central nervous system.
3. **Motor neurons** (efferent neurons) are multipolar and conduct impulses out of the brain or spinal cord to effectors. Motor impulses control muscle contraction and the secretions of glands.

Neurons deprived of oxygen change shape as their nuclei shrink, and they eventually disintegrate. Oxygen deficiency can result from lack of blood flow (ischemia) through nervous tissue, an abnormally low blood oxygen concentration (hypoxemia), or toxins that prevent neurons from using oxygen by blocking aerobic respiration.

## PRACTICE

9. Distinguish between a dendrite and an axon.
10. Describe the components of a neuron.
11. Describe how a myelin sheath forms.
12. Explain why axons of peripheral nerves can regenerate, but axons of central nervous system nerves cannot.
13. Name three groups of neurons based on structure and three groups based on function.

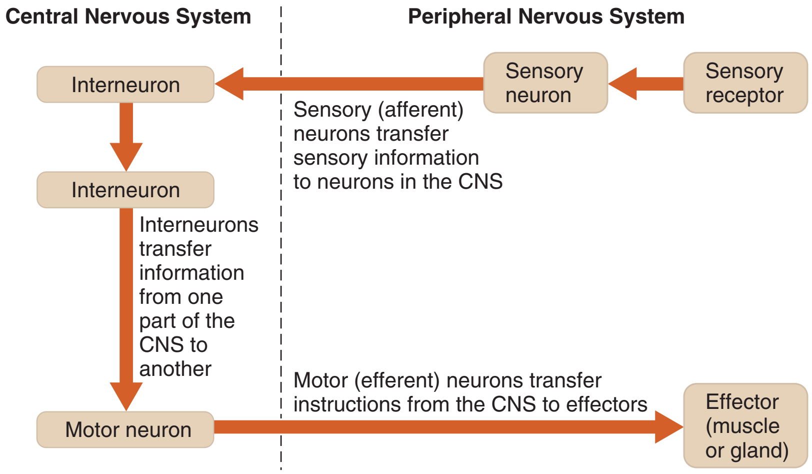

Central Nervous System
Peripheral Nervous System
Interneuron
Sensory neuron
Sensory receptor
Sensory (afferent) neurons transfer sensory information to neurons in the CNS
Interneuron
Interneurons transfer information from one part of the CNS to another
Motor (efferent) neurons transfer instructions from the CNS to effectors
Motor neuron
Effector (muscle or gland)

**FIGURE 9.7** Neurons are classified by function as well as structure. Sensory (afferent) neurons carry information into the central nervous system (CNS), interneurons are completely within the CNS, and motor (efferent) neurons carry instructions to the effectors.

## 9.5 | The Synapse

As in the case of a motor neuron and a skeletal muscle fiber, the functional connection between two neurons is called a **synapse**. The neurons at a synapse are not in direct physical contact, but are separated by a gap called a *synaptic cleft.* Communication along a nerve pathway must cross these gaps (fig. 9.8).

When you receive a text message, the person texting is the sender and you are the receiver. Similarly, the neuron conducting the impulse to the synapse is the sender, or *presynaptic neuron.* The neuron that receives input at the synapse is the receiver, or *postsynaptic neuron.* The process whereby this message crosses the synaptic cleft is called *synaptic transmission.* Clinical Application 9.1 discusses some factors that affect synaptic transmission.

Synaptic transmission is a one-way process carried out by biochemicals called **neurotransmitters.** The distal ends of axons have one or more extensions called *synaptic knobs,* absent in dendrites, which contain many membranous sacs called *synaptic vesicles.* When an impulse reaches a synaptic knob, some of the synaptic vesicles release neurotransmitter (figs. 9.9 and 9.10). The neurotransmitter diffuses across the synaptic cleft and reacts with specific receptors on the postsynaptic neuron membrane.

Once the neurotransmitter binds to receptors on a postsynaptic cell, the effect is either excitatory (stimulating an impulse) or inhibitory (preventing an impulse). The net effect on the postsynaptic cell depends on the combined effect of the excitatory and inhibitory inputs from as few as one and as many as 10,000 presynaptic neurons.

## 9.6 | Cell Membrane Potential

The surface of a cell membrane (including a nonstimulated or *resting* neuron) is usually electrically charged, or *polarized,* with respect to the inside. This polarization arises from an unequal distribution of positive and negative ions across the membrane, and it is particularly important in the conduction of impulses in muscle cells and neurons. A characteristic change in neuron membrane polarization and return to the resting state, called an *action potential,* forms an impulse that is propagated along an axon.

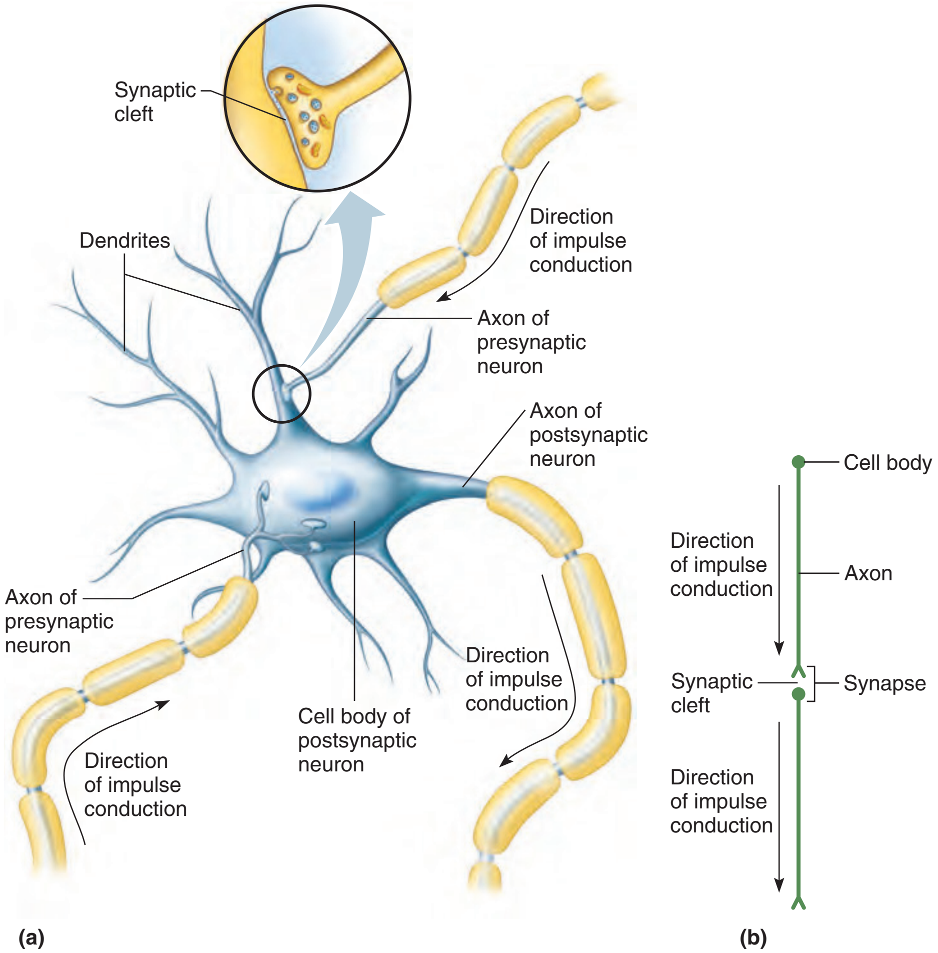

Synaptic cleft
Dendrites
Direction of impulse conduction
Axon of presynaptic neuron
Axon of postsynaptic neuron
Axon of presynaptic neuron
Direction of impulse conduction
Cell body of postsynaptic neuron
Direction of impulse conduction
(a)
Cell body
Direction of impulse conduction
Axon
Synaptic cleft
Synapse
Direction of impulse conduction
(b)

**FIGURE 9.8** APR Synapses separate neurons. **(a)** For an impulse to continue on a postsynaptic neuron, neurotransmitter must cross the synapse and stimulate the postsynaptic neuron. A synapse is usually between an axon and a dendrite or between an axon and a cell body. **(b)** A schematic representation of presynaptic and postsynaptic neurons.

## Distribution of Ions

Because of the active transport of sodium and potassium ions, cells throughout the body have a greater concentration of sodium ions ($Na^+$) outside and a greater concentration of potassium ions ($K^+$) inside (see chapter 3, pp. 75–76). The cytoplasm of these cells has many large, negatively charged particles, including phosphate ions ($PO_4^{-3}$), sulfate ions ($SO_4^{-2}$), and proteins, that cannot diffuse across the cell membranes.

Chapter 3 (p. 62) introduced cell membranes as selectively permeable phospholipid bilayers. Channels in the cell membranes partly determine the distribution of ions inside and outside of cells (see chapter 3, p. 64). Some channels are always open. Others, called "gated" channels, can be opened or closed. Furthermore, channels can be selective; that is, a channel may allow one kind of ion to pass through and exclude other kinds (fig. 9.11).

Potassium ions pass through cell membranes much more easily than sodium ions. This makes potassium ions a major contributor to membrane polarization. Calcium ions are less able to cross the resting cell membrane than either sodium ions or potassium ions, and have a special role in nerve function, described on page 239.

## Resting Potential

Sodium and potassium ions follow the laws of diffusion discussed in chapter 3 (pp. 70–73) and show a net movement from high concentration to low concentration as permeabilities permit. Because a resting cell membrane is more permeable to potassium ions than to sodium ions, potassium ions diffuse out of the cell more rapidly than sodium ions can diffuse in (fig. 9.12*a*). Every millisecond, more positive charges leave the cell by diffusion than enter it. As a result, the outside of the

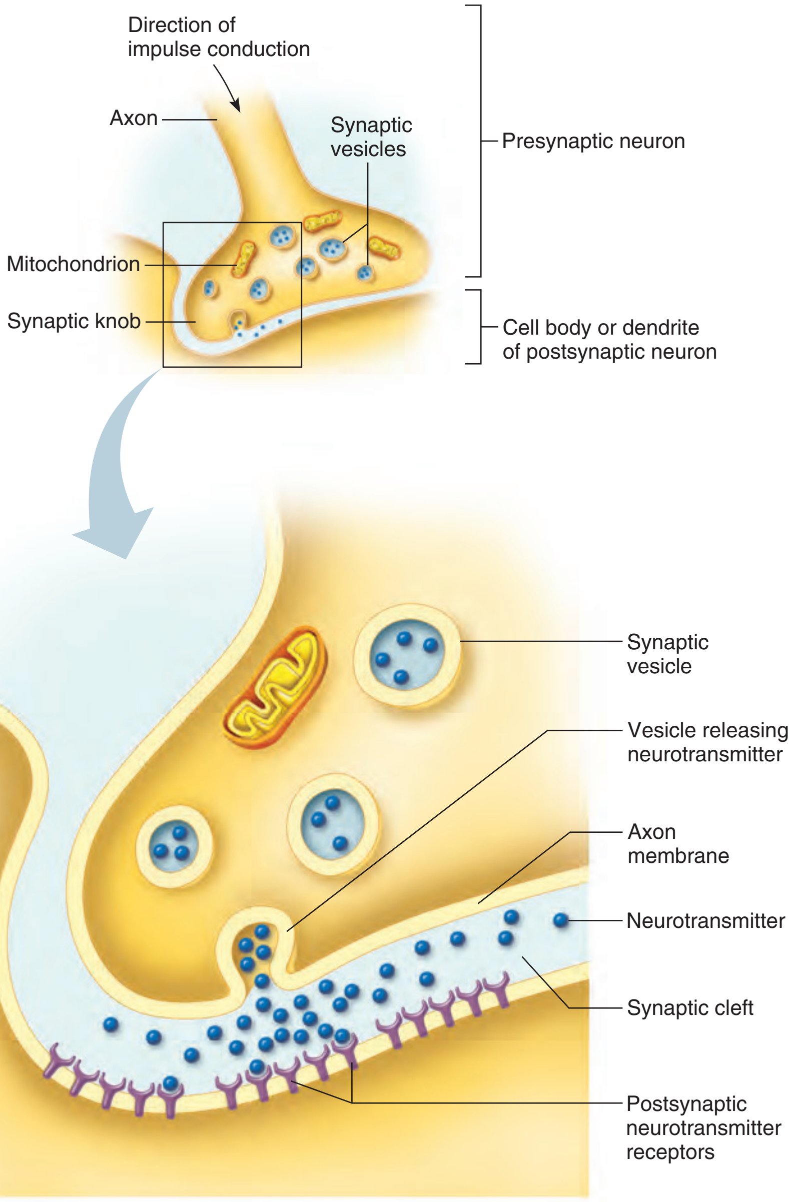

Direction of impulse conduction
Axon
Synaptic vesicles
Presynaptic neuron
Mitochondrion
Synaptic knob
Cell body or dendrite of postsynaptic neuron
Synaptic vesicle
Vesicle releasing neurotransmitter
Axon membrane
Neurotransmitter
Synaptic cleft
Postsynaptic neurotransmitter receptors

**FIGURE 9.9** APIR Action across a synapse. When an impulse reaches the synaptic knob at the end of an axon, synaptic vesicles release a neurotransmitter that diffuses across the synaptic cleft and binds to specific receptors on the membrane of the postsynaptic cell.

### CLINICAL APPLICATION 9.1

## Factors Affecting Synaptic Transmission

Impulses reaching synaptic knobs too rapidly can exhaust neurotransmitter supplies, and impulse conduction ceases until more neurotransmitters are synthesized. This happens during an epileptic seizure. Abnormal and too rapid impulses originate from certain brain cells and reach skeletal muscle fibers, stimulating violent contractions. In time, the synaptic knobs run out of neurotransmitters and the seizure subsides.

A drug called Dilantin (diphenylhydantoin) treats seizure disorders by blocking gated sodium channels, thereby limiting the frequency at which action potentials can occur. Many other drugs affect synaptic transmission. For example, caffeine in coffee, tea, and cola drinks stimulates nervous system activity by lowering the thresholds at synapses so that neurons are more easily excited. Antidepressants called "selective serotonin reuptake inhibitors" keep the neurotransmitter serotonin in synapses longer, compensating for a still little-understood deficit that presumably causes depression.

cell membrane gains a slight surplus of positive charges, and the inside is left with a slight surplus of impermeant negative charges (fig. 9.12*b*).

The difference in electrical charge between two regions is called a *potential difference.* In a resting nerve cell, the potential difference between the region inside the membrane and the region outside the membrane is called a **resting potential.** As long as a nerve cell membrane is undisturbed, the membrane remains in this polarized state. At the same time, the cell continues to expend energy to drive the $Na^+/K^+$ "pumps" that actively transport sodium and potassium ions in opposite directions. The pump maintains the concentration gradients responsible for diffusion of these ions in the first place (fig. 9.12*c*).

Recall from chapter 5 (p. 122) that neurons can conduct electrical signals. The key to understanding how this happens is the **action potential**, which is a rapid change in the membrane potential, first in a positive direction, then in a negative direction, returning to the resting potential (figure 9.13). When a neuron conducts an electrical current, that current is in the form of a

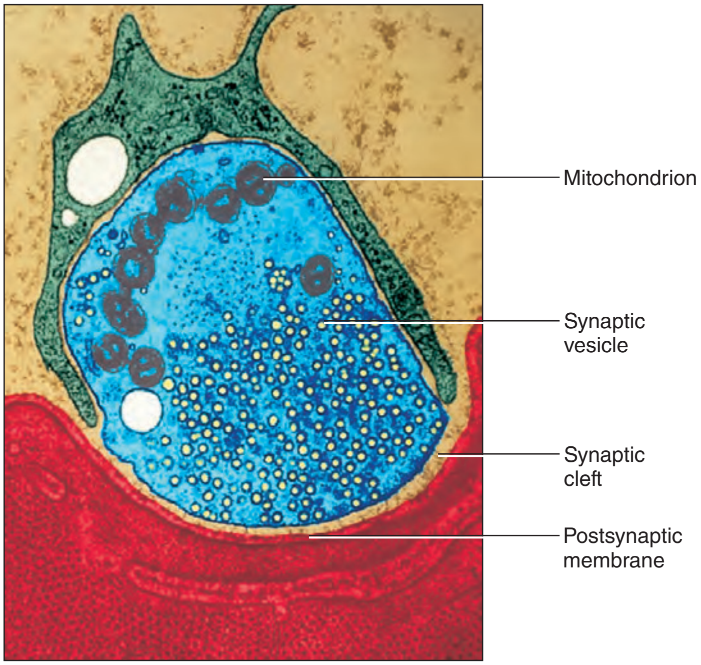
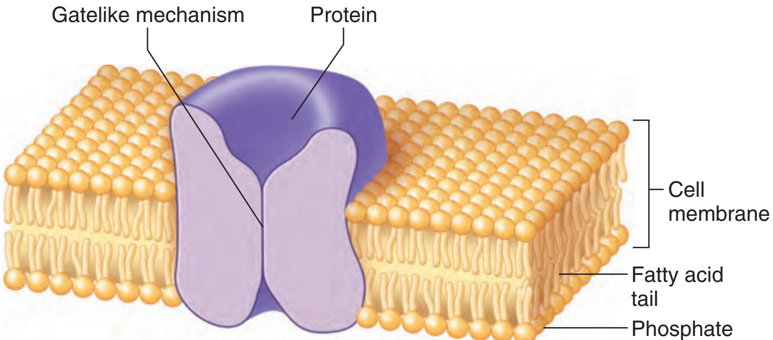
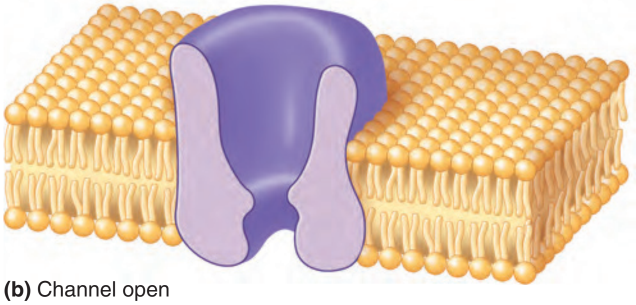


**FIGURE 9.10** This transmission electron micrograph of a synaptic knob shows abundant synaptic vesicles, which are filled with neurotransmitter molecules (37,500x).

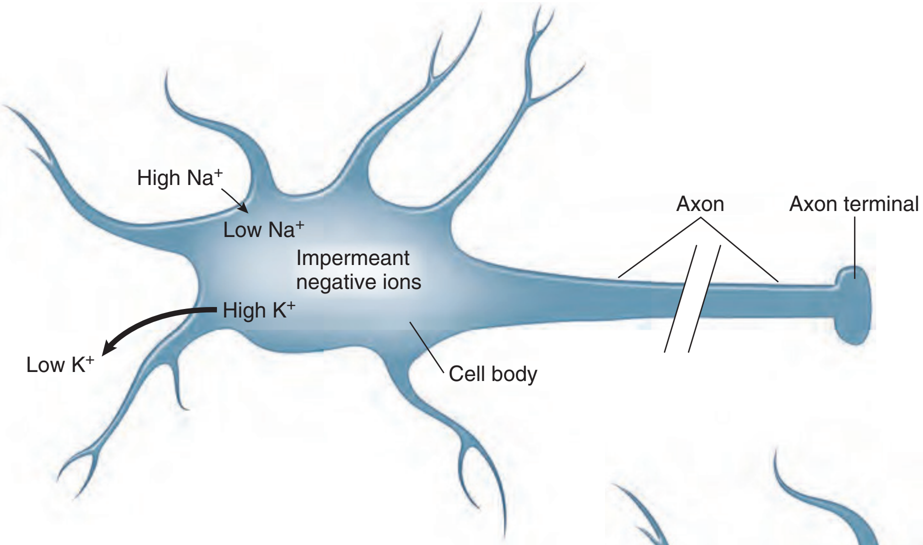


**(a)** Channel closed

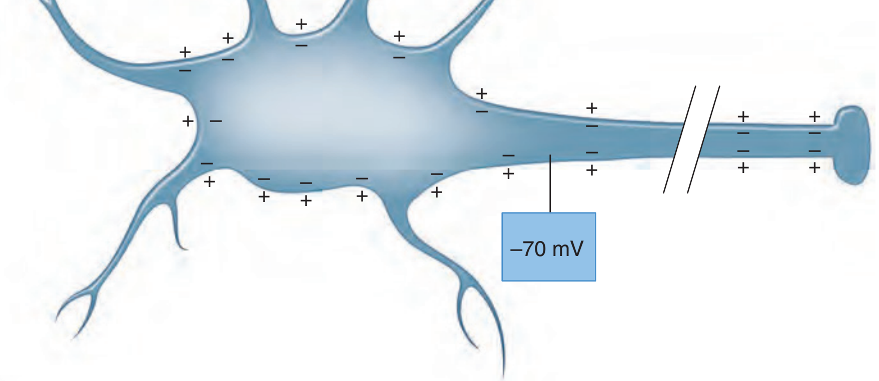


**(b)** Channel open

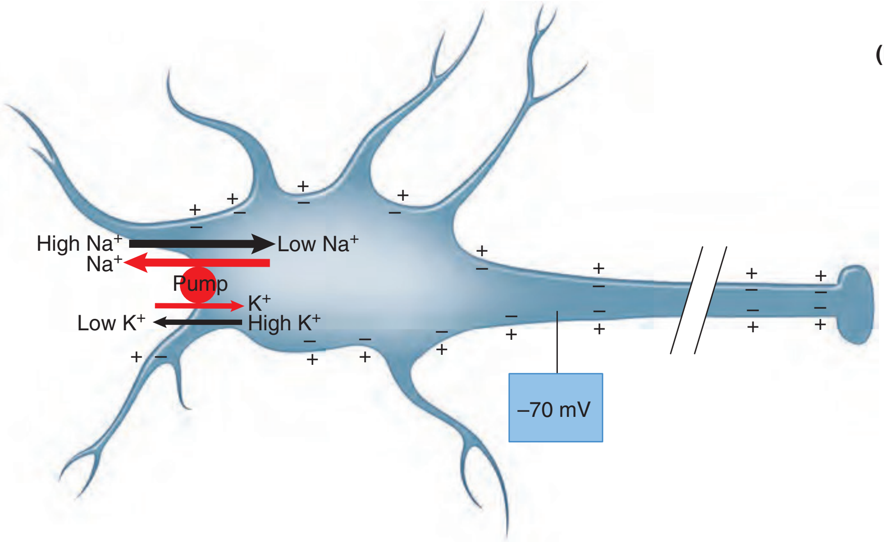
**FIGURE 9.11** Channels in cell membranes partly determine the distribution of ions inside and outside of cells. A gatelike mechanism can **(a)** close or **(b)** open some of the channels in cell membranes through which ions pass.



**(a)** If we imagine a neuron before the membrane potential is established, concentration gradients are such that diffusion of potassium ions out of the cell exceeds diffusion of sodium ions into the cell, causing a net loss of positive charge from the cell.



**(b)** The net loss of positive charges from the inside of the cell has left the inside of the cell membrane slightly negative compared to the outside of the membrane, which is left slightly positive. This difference (an electrical "potential difference") is measured as –70 millivolts (mV) in a typical neuron, and is called the resting membrane potential.



**(c)** With the membrane potential established, sodium diffusion into the cell is now aided, and potassium diffusion opposed, by the negative charge on the inside of the membrane. As a result, slightly more sodium ions enter the cell than potassium ions leave, but the action of the sodium/potassium pump balances these movements, and as a result the concentrations of these ions, and the resting membrane potential, are maintained.

**FIGURE 9.12** The resting potential. **(a)** Conditions that lead to the resting potential. **(b)** In the resting neuron, the inside of the membrane is negative relative to the outside. **(c)** The Na$^+$/K$^+$ pump maintains the concentration gradients for Na$^+$ and K$^+$ ions.

**Q** *Constant activity of the Na$^+$/K$^+$ pump requires a constant supply of which substance?*

**Answer can be found in Appendix F on page 582.**

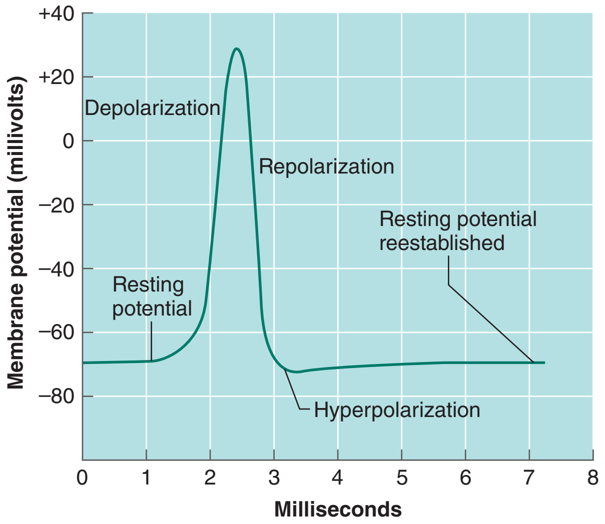


**FIGURE 9.13** A recording of an action potential.

series of action potentials occurring in sequence along the axon, from the cell body to the axon terminal. The next sections discuss how all of this happens.

## Potential Changes

Nerve cells are excitable; that is, they can respond to changes in their surroundings. Some nerve cells, for example, are specialized to detect changes in temperature, light, or pressure from outside the body. Many neurons respond to neurotransmitters from other neurons. Such changes (or stimuli) usually affect the resting potential in a particular region of a nerve cell membrane. If the membrane's resting potential decreases (as the inside of the membrane becomes less negative when compared to the outside), the membrane is said to be *depolarized* (fig. 9.14*a*).

Local potential changes are graded. This means that the magnitude of change in the resting potential is directly proportional to the intensity of the stimulus. That is, if the membrane is being depolarized, then the greater the stimulus, the greater the depolarization. If, and only if, neurons are depolarized sufficiently, the membrane potential reaches a level called the **threshold potential,** which is approximately −55 millivolts. If threshold is reached, an **action potential** results (figs. 9.14*b* and 9.15).

## Action Potential

Recall that the axon arises from the cell body as a thickened cone-shaped region called the axon hillock. Functionally, this region is referred to as the trigger zone. At the threshold potential, permeability changes at the trigger zone of the neuron being stimulated. Here, gated channels sensitive to changes in membrane potential, and highly selective for sodium ions, open and allow sodium to diffuse freely inward (figs. 9.14*b* and 9.15*b*). The negative electrical condition on the inside of the membrane aids this movement by attracting the positively-charged sodium ions.

As sodium ions diffuse inward, inside the membrane loses its negative electrical charge and becomes depolarized (more positive). At almost the same time, however, gated membrane channels open that allow potassium ions to pass through, and as these positive ions diffuse outward, the inside of the membrane becomes negatively charged once more (fig. 9.15*c*). The membrane potential may briefly become overly negative (*hyperpolarization*), but the membrane quickly returns to the resting potential (*repolarization*), and it remains in this state until stimulated again.

This rapid sequence of depolarization and repolarization, which takes about one-thousandth of a second (one millisecond), is the action potential (see fig. 9.13). Because only a small fraction of the sodium and potassium ions move through the membrane during an action potential, action potentials can occur again and again, and resting potentials can be reestablished, before the original concentrations of these ions change significantly. Also, active transport across the membrane maintains the original concentrations of sodium and potassium ions on either side.

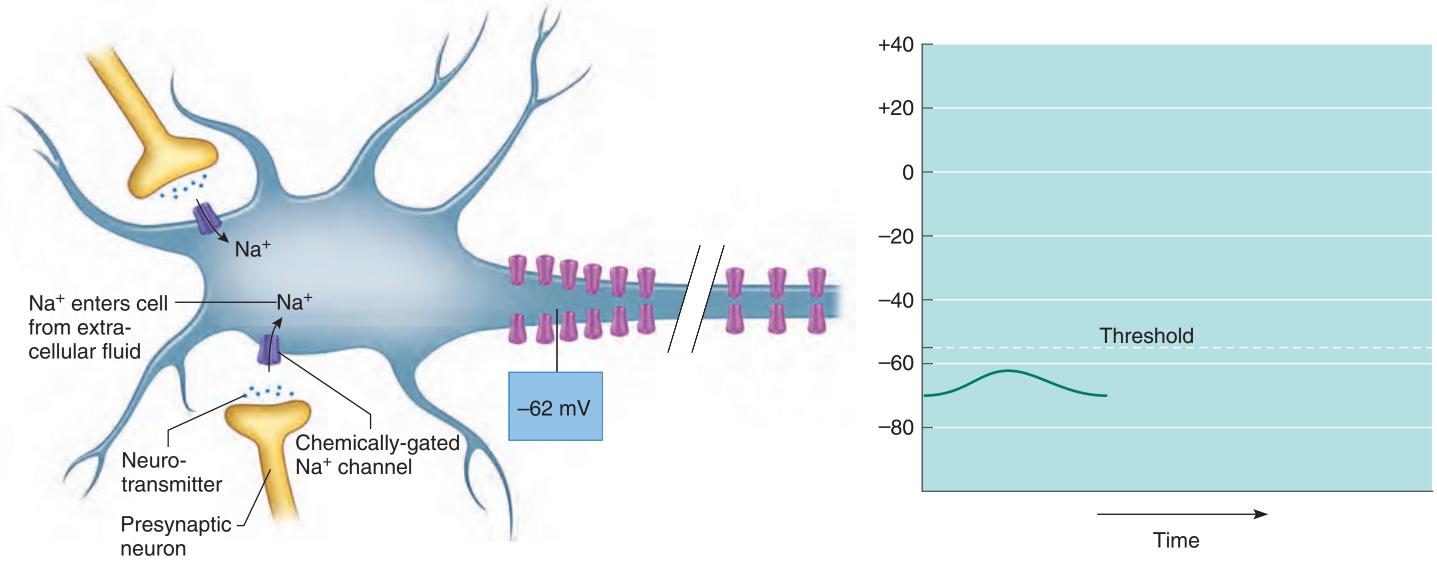
**PRACTICE**

14. Describe the events that occur at a synapse.
15. Summarize how a nerve fiber becomes polarized.
16. List the major events of an action potential.

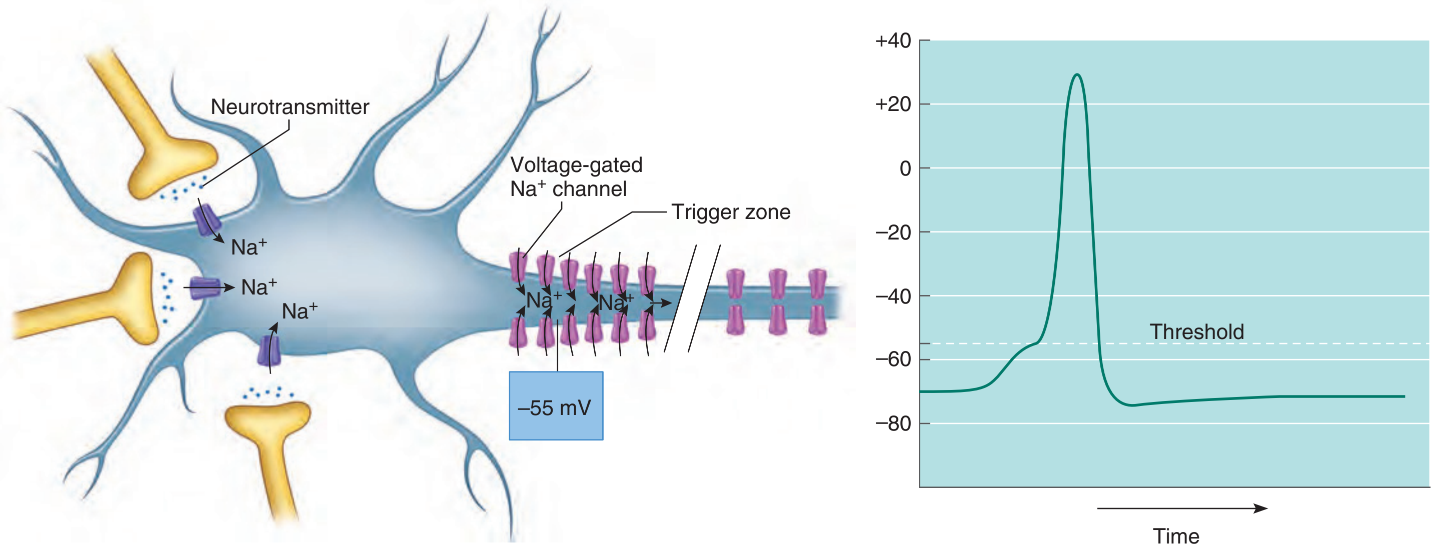
## 9.7 | Impulse Conduction

Axons are capable of action potentials, but the cell bodies and dendrites of most neurons are not. An action potential at the trigger zone of an axon causes a bioelectric current to flow to adjacent regions of the axon membrane. This *local current* stimulates the adjacent membrane to its threshold level and triggers another action potential. This, in turn, stimulates the next adjacent region. In this way, a wave of action potentials moves down the axon to the end (fig. 9.16). Table 9.1 summarizes the conduction of an impulse.

An unmyelinated axon conducts an impulse along its entire length. A myelinated axon functions differently because myelin insulates and prevents almost all ion flow through the membrane it encloses. The myelin sheath would prevent an impulse altogether if the sheath was continuous. However, nodes of Ranvier between Schwann cells interrupt the sheath (see fig. 9.4). Action potentials occur at these nodes,


Na⁺
Na⁺ enters cell from extra-cellular fluid
Na⁺
Neuro-transmitter
Presynaptic neuron
Chemically-gated Na⁺ channel
–62 mV
+40
+20
0
–20
–40
–60
–80
Threshold
Time

**(a)** If sodium or potassium channels open, more of that particular ion will cross the cell membrane, and the resting membrane potential will be altered. Here we see the effect of sodium channels opening in response to a neurotransmitter. As sodium ions enter the cell, the membrane potential becomes more positive (or less negative), changing from –70 millivolts to –62 millivolts in this example. This change in a positive direction is called depolarization. In this case it is a subthreshold depolarization, and does not generate an action potential.


Neurotransmitter
Na⁺
Na⁺
Na⁺
Voltage-gated Na⁺ channel
Trigger zone
Na⁺
Na⁺
–55 mV
+40
+20
0
–20
–40
–60
–80
Threshold
Time

**(b)** If enough sodium ions enter the cell, and the membrane potential depolarizes to a value called threshold (here shown to be –55 millivolts), a threshold depolarization causes another type of sodium channel to open. These channels are found along the axon of the neuron, especially near the beginning in an area known as the “trigger zone,” and their opening is what triggers the action potential.

**FIGURE 9.14** APR Action potentials. **(a)** A subthreshold depolarization will not result in an action potential. **(b)** Stimulation from multiple presynaptic neurons may cause the postsynaptic neuron to reach threshold, opening voltage-gated channels at the trigger zone.

where the exposed axon membrane has sodium and potassium channels. In this case, the adjacent membrane that is brought to threshold is at the next node down the axon. An impulse traveling along a myelinated axon thus appears to jump from node to node. This type of impulse conduction, termed saltatory, is many times faster than conduction on an unmyelinated axon.

The speed of an impulse is proportional to the diameter of the axon—the greater the diameter, the faster the impulse. For example, an impulse on a relatively thick myelinated axon, such as that of a motor neuron associated with a skeletal muscle, might travel 120 meters per second. An impulse on a thin, unmyelinated axon, such as that of a sensory neuron associated with the skin, might move only 0.5 meter per second.

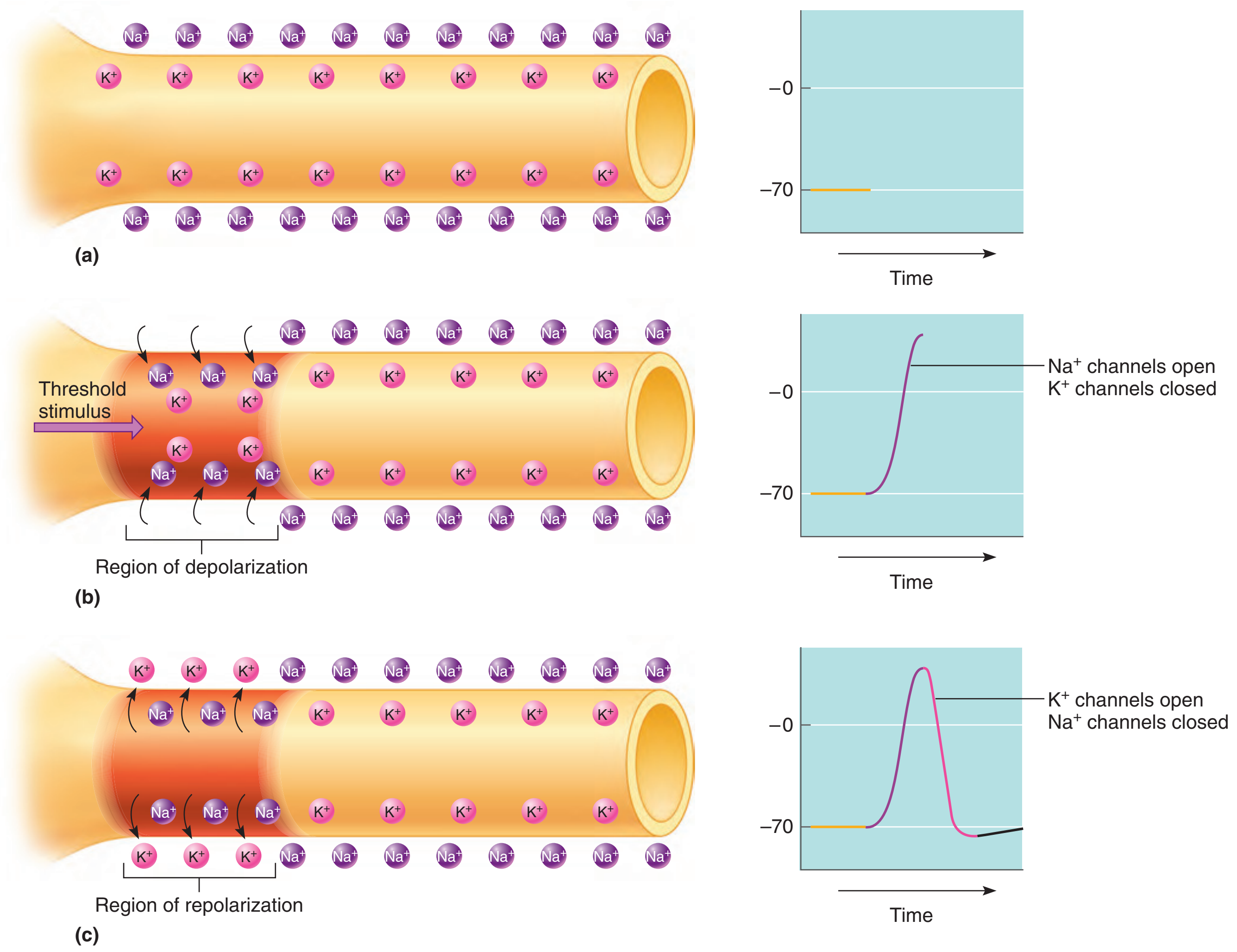


**FIGURE 9.15** APR Action potential. **(a)** At rest, the membrane potential is negative. **(b)** When the membrane reaches threshold, sodium channels open, some sodium ($Na^+$) diffuses into the axon, and the membrane is depolarized. **(c)** Soon afterward, potassium channels open, potassium ($K^+$) diffuses out of the axon, and the membrane is repolarized. (For simplicity, negative ions are not shown.)

**TABLE 9.1 Conduction of an Impulse**

1. Neuron membrane maintains resting potential.
2. Threshold stimulus is received.
3. Sodium channels in the trigger zone of the axon open.
4. Sodium ions diffuse inward, depolarizing the axon membrane.
5. Potassium channels in the axon membrane open.
6. Potassium ions diffuse outward, repolarizing the axon membrane.
7. The resulting action potential causes a local bioelectric current that stimulates adjacent portions of the axon membrane.
8. A wave of action potentials travels the length of the axon as an impulse.

## All-or-None Response

An action potential is not graded; rather it is an *all-or-none response.* That is, if a neuron responds at all, it responds completely. Thus, an action potential occurs whenever a stimulus of threshold intensity or above is applied to an axon, and all action potentials propagated on that axon are of the same strength. A greater intensity of stimulation does not produce a stronger action potential; instead it produces more action potentials per second.

For a very short time following an action potential, a threshold stimulus will not trigger another action potential on that axon. This brief period, called the *refractory period,* limits the frequency of action potentials, along an

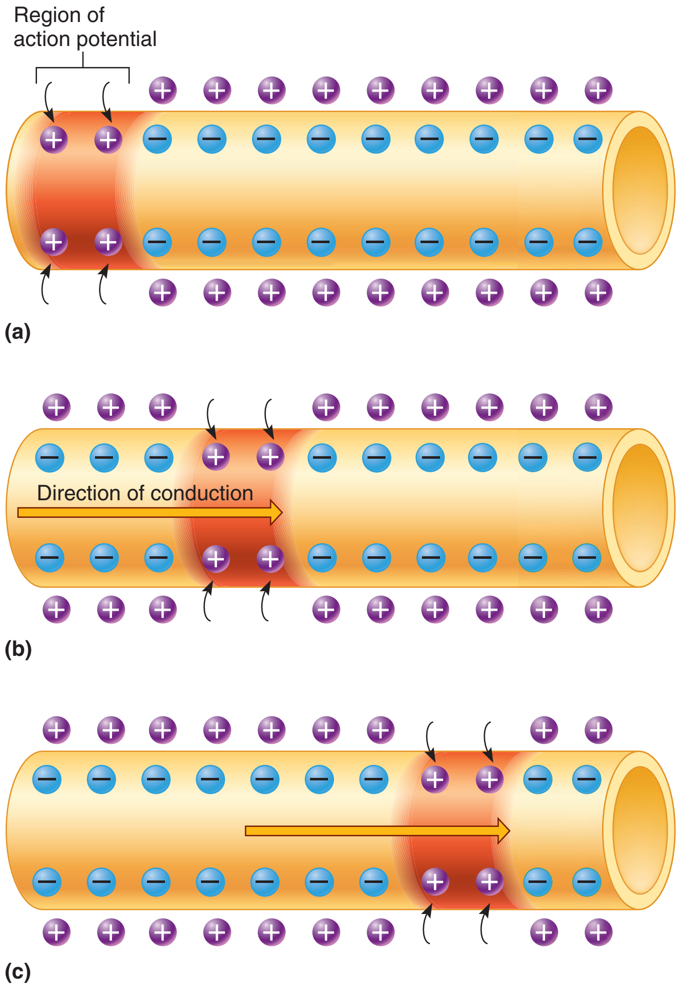


**FIGURE 9.16** APIR Conduction of an impulse. **(a)** An action potential in one region stimulates the adjacent region, and **(b)** and **(c)** a wave of action potentials (an impulse) moves along the axon.

axon. It also ensures that the impulse is conducted in only one direction—down the axon, because the area upstream from where the action potential has just occurred is still in the refractory period from the previous action potential. Although a frequency of 700 impulses per second is possible, 100 impulses per second is more common.

**PRACTICE**

17. What is the relationship between action potentials and impulses?
18. Explain how impulse conduction differs in myelinated and unmyelinated nerve fibers.
19. Define *all-or-none response* as it relates to impulse conduction.

## 9.8 | Synaptic Transmission

Neurotransmitters have various effects when they diffuse across the synaptic cleft and react with specific receptor molecules in the postsynaptic neuron membrane.

### Excitatory and Inhibitory Actions

Neurotransmitters that increase postsynaptic membrane permeability to sodium ions will bring the postsynaptic membrane closer to threshold and may trigger impulses. Such neurotransmitters are **excitatory.** Neurotransmitters that make reaching threshold less likely are called **inhibitory,** because they decrease the chance that an impulse will occur.

The synaptic knobs of a thousand or more neurons may communicate with the dendrites and cell body of a single postsynaptic neuron. Neurotransmitters released by some of these knobs have an excitatory action, while those from other knobs have an inhibitory action. The overall effect on the postsynaptic neuron depends on which presynaptic knobs are activated from moment to moment. If more excitatory than inhibitory neurotransmitters are released, the postsynaptic neuron's threshold may be reached, and an action potential triggered. Conversely, if most of the neurotransmitters released are inhibitory, threshold may not be reached.

### Neurotransmitters

More than 100 neurotransmitters have been identified in the nervous system. Some neurons release only one, while others produce two or three. The neurotransmitters include *acetylcholine,* which stimulates skeletal muscle contractions (see chapter 8, p. 193); a group of compounds called *biogenic amines* (such as epinephrine, norepinephrine, dopamine, and serotonin), which form from modified amino acids; several *amino acids* (such as glycine, glutamic acid, aspartic acid, and gamma-aminobutyric acid—GABA); and more than 50 *neuropeptides,* which are short chains of amino acids. Acetylcholine and norepinephrine are excitatory. GABA and glycine are inhibitory. Neurotransmitters are usually synthesized in the cytoplasm of the synaptic knobs and stored in the synaptic vesicles. Table 9.2 lists some neurotransmitters and their actions.

When an action potential reaches the membrane of a synaptic knob, it increases the membrane's permeability to calcium ions by opening calcium ion channels in the membrane. Consequently, calcium ions diffuse inward, and in response some synaptic vesicles fuse with the membrane and release their contents into the synaptic cleft. After being released, some neurotransmitters are decomposed by enzymes. For example, the enzyme *acetylcholinesterase* decomposes acetylcholine and is present in the synapse and on the postsynaptic

**TABLE 9.2** Some Neurotransmitters and Representative Actions

| Neurotransmitter | Location | Major Actions |
|---|---|---|
| Acetylcholine | CNS | Controls skeletal muscle actions |
| | PNS | Stimulates skeletal muscle contraction at neuromuscular junctions; may excite or inhibit at autonomic nervous system synapses |
| *Monoamines* | | |
| Norepinephrine | CNS | Creates a sense of feeling good; low levels may lead to depression |
| | PNS | May excite or inhibit autonomic nervous system actions, depending on receptors |
| Dopamine | CNS | Creates a sense of feeling good; deficiency in some brain areas is associated with Parkinson disease |
| | PNS | Limited actions in autonomic nervous system; may excite or inhibit, depending on receptors |
| Serotonin | CNS | Primarily inhibitory; leads to sleepiness; action is blocked by LSD, enhanced by selective serotonin reuptake inhibitor drugs |
| Histamine | CNS | Release in hypothalamus promotes alertness |
| *Amino acids* | | |
| GABA | CNS | Generally inhibitory |
| Glutamic acid | CNS | Generally excitatory |
| *Neuropeptides* | | |
| Substance P | PNS | Excitatory; pain perception |
| Endorphins, enkephalins | CNS | Generally inhibitory; reduce pain by inhibiting substance P release |
| *Gases* | | |
| Nitric oxide | PNS | Vasodilation |
| | CNS | May play a role in memory |

membrane of neuromuscular junctions, which control skeletal muscle contraction. Other neurotransmitters are transported back into the synaptic knob that released them (reuptake) or into nearby neurons or neuroglia. Decomposition or removal of neurotransmitters prevents continuous stimulation of postsynaptic neurons. Table 9.3 summarizes the events leading to the release of a neurotransmitter.

**PRACTICE**

20. Distinguish between the actions of excitatory and inhibitory neurotransmitters.
21. What types of chemicals function as neurotransmitters?
22. What are possible fates of neurotransmitters?

## 9.9 | Impulse Processing

The way the nervous system processes and responds to impulses reflects, in part, the organization of neurons and their axons in the brain and spinal cord.

**TABLE 9.3** Events Leading to the Release of a Neurotransmitter

1. Action potential passes along an axon and over the surface of its synaptic knob.
2. Synaptic knob membrane becomes more permeable to calcium ions, and they diffuse inward.
3. In the presence of calcium ions, synaptic vesicles fuse to synaptic knob membrane.
4. Synaptic vesicles release their neurotransmitter into synaptic cleft.

### Neuronal Pools

Neurons in the CNS are organized into **neuronal pools.** These are groups of neurons that make hundreds of synaptic connections with each other and work together to perform a common function. Each pool receives input from neurons (which may be part of other pools), and each pool generates output. Neuronal pools may have excitatory or inhibitory effects on other pools or on peripheral effectors.

## Facilitation

As a result of incoming impulses and neurotransmitter release, a particular neuron of a neuronal pool may receive excitatory and inhibitory input. If the net effect of the input is excitatory, threshold may be reached, and an outgoing impulse triggered. If the net effect is excitatory but subthreshold, an impulse is not triggered, but another immediate release of neurotransmitter will be more likely to bring the postsynaptic cell to threshold. This is called **facilitation** (fah-sil″ĭ-ta′shun).

## Convergence

Any single neuron in a neuronal pool may receive impulses from two or more incoming axons. Axons originating from different parts of the nervous system and leading to the same neuron exhibit **convergence** (kon-ver′jens) (fig. 9.17*a*).

Convergence makes it possible for impulses arriving from different sources to have an additive effect on a neuron. For example, if a neuron is facilitated by receiving subthreshold stimulation from one input neuron, it may reach threshold if it receives additional stimulation from a second input neuron. As a result, an impulse may travel to a particular effector and evoke a response.

Incoming impulses often bring information from several sensory receptors that detect changes. Convergence allows the nervous system to collect a variety of kinds of information, process it, and respond to it in a special way.

## Divergence

Impulses leaving a neuron of a neuronal pool often exhibit **divergence** (di-ver′jens) by passing into several other output neurons (fig. 9.17*b*). For example, an impulse from one neuron may stimulate two others; each of these, in turn, may stimulate several others, and so forth. Divergence can amplify an impulse—that is, spread it to more neurons in the pool. As a result of divergence, an impulse originating from a single neuron in the CNS may be amplified so that impulses reach enough motor units within a skeletal muscle to cause forceful contraction (see chapter 8, pp. 199–200). Similarly, an impulse originating from a sensory receptor may diverge and reach several different regions of the CNS, where the resulting impulses are processed and acted upon.

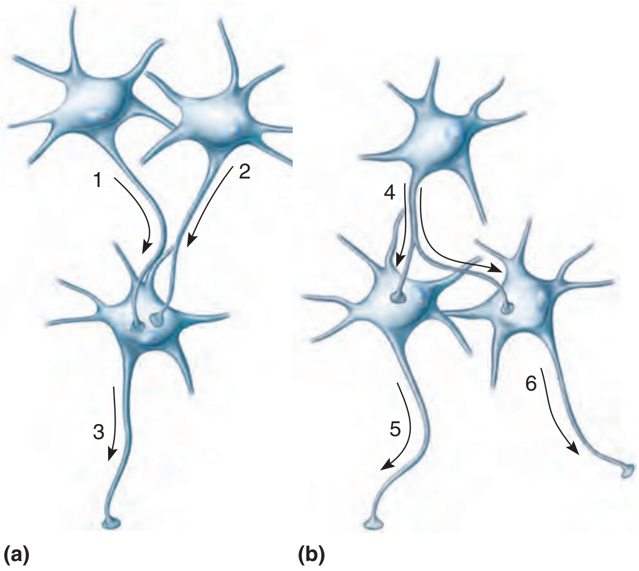


**FIGURE 9.17** Impulse processing in neuronal pools. **(a)** Axons of neurons 1 and 2 converge to the cell body of neuron 3. **(b)** The axon of neuron 4 diverges to the cell bodies of neurons 5 and 6.

**PRACTICE**

23. Define *neuronal pool*.
24. Distinguish between convergence and divergence.

## 9.10 | Types of Nerves

Recall from section 9.1 (p. 224) that nerves are bundles of axons. An axon is often referred to as a nerve fiber. Because of this, we will refer to the neuron processes that bring sensory information into the CNS as **sensory fibers,** or **afferent fibers.** In contrast, **motor fibers** or **efferent fibers** carry impulses from the CNS to effectors (muscles or glands). A nerve is a cordlike bundle (or group of bundles) of nerve fibers within layers of connective tissue (fig. 9.18).

The terminology used to describe muscle and nerve fibers is somewhat inconsistent. "Muscle fiber" refers to a muscle cell, whereas "nerve fiber" refers to an axon, which is part of a cell. However, names for the associated connective tissues are similar. Both muscle and nerve fibers are bundled into fascicles. Recall from figure 8.1 (pp. 189–190) that epimysium, perimysium, and endomysium connective tissue separates muscle tissue into compartments. Similarly, a nerve is defined by an outer *epineurium,* with *perineurium* surrounding a nerve fascicle within the nerve, and *endoneurium* surrounding an individual nerve fiber.

Like neurons, nerves that conduct impulses to the brain or spinal cord are called **sensory nerves,** and those that carry impulses to muscles or glands are termed **motor nerves.** Most nerves include both sensory and motor fibers and are called **mixed nerves.**

**PRACTICE**

25. What is a nerve?
26. How does a mixed nerve differ from a sensory nerve? From a motor nerve?

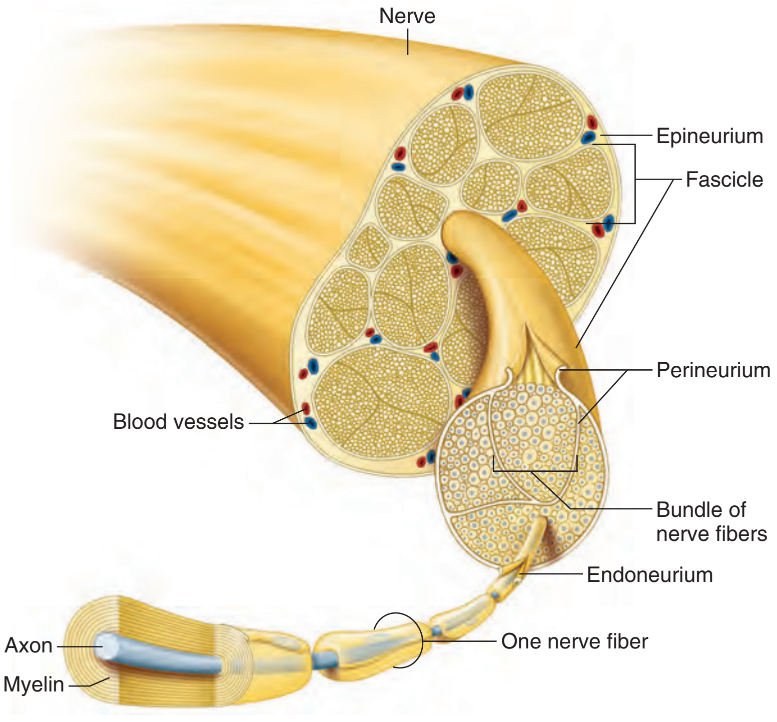


**FIGURE 9.18** Connective tissue binds a bundle of nerve fibers, forming a fascicle. Many fascicles form a nerve.

## 9.11 | Nerve Pathways

The routes impulses follow as they travel through the nervous system are called *nerve pathways.* The simplest of these pathways includes only a few neurons and is called a **reflex** (re′fleks) **arc.** It constitutes the structural and functional basis for involuntary actions called **reflexes.**

### Reflex Arcs

A reflex arc begins with a receptor at the end of a sensory (or afferent) neuron. This neuron usually leads to several interneurons in the CNS, which serve as a processing center, or *reflex center.* These interneurons can connect with interneurons in other parts of the nervous system. They also communicate with motor (or efferent) neurons, whose axons pass outward from the CNS to effectors, usually muscles or glands (fig. 9.19).

### Reflex Behavior

Reflexes are automatic responses to changes (stimuli) within or outside the body. They help maintain homeostasis by controlling many involuntary processes, such as heart rate, breathing rate, blood pressure, and digestion. Reflexes also carry out the automatic actions of swallowing, sneezing, coughing, and vomiting.

The *patellar reflex* (knee-jerk reflex) is an example of a simple reflex involving a pathway of only two neurons—a sensory neuron communicating directly with a motor neuron. Striking the patellar ligament just below the patella initiates this reflex. The quadriceps femoris muscle group, which is attached to the patella by a tendon, is pulled slightly, stimulating stretch receptors in these muscles. These receptors, in turn, trigger impulses that pass along the axon of a sensory neuron into the spinal cord. Within the spinal cord, the sensory axon synapses with a motor neuron. An impulse is then triggered along the axon of the motor neuron and travels back to the quadriceps femoris group. The muscle group contracts in response, and the reflex is completed as the leg extends (fig. 9.20).

The patellar reflex helps maintain upright posture. If the knee begins to bend from the force of gravity when a person is standing still, the quadriceps femoris group is stretched, the reflex is triggered, and the leg straightens again.

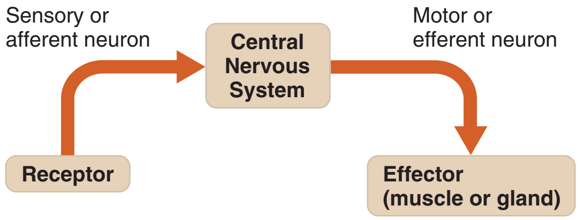


**FIGURE 9.19** APR A reflex arc is the simplest nerve pathway. It involves a sensory neuron that sends a message to the CNS, and a motor neuron that sends the message from the CNS to a muscle or gland.

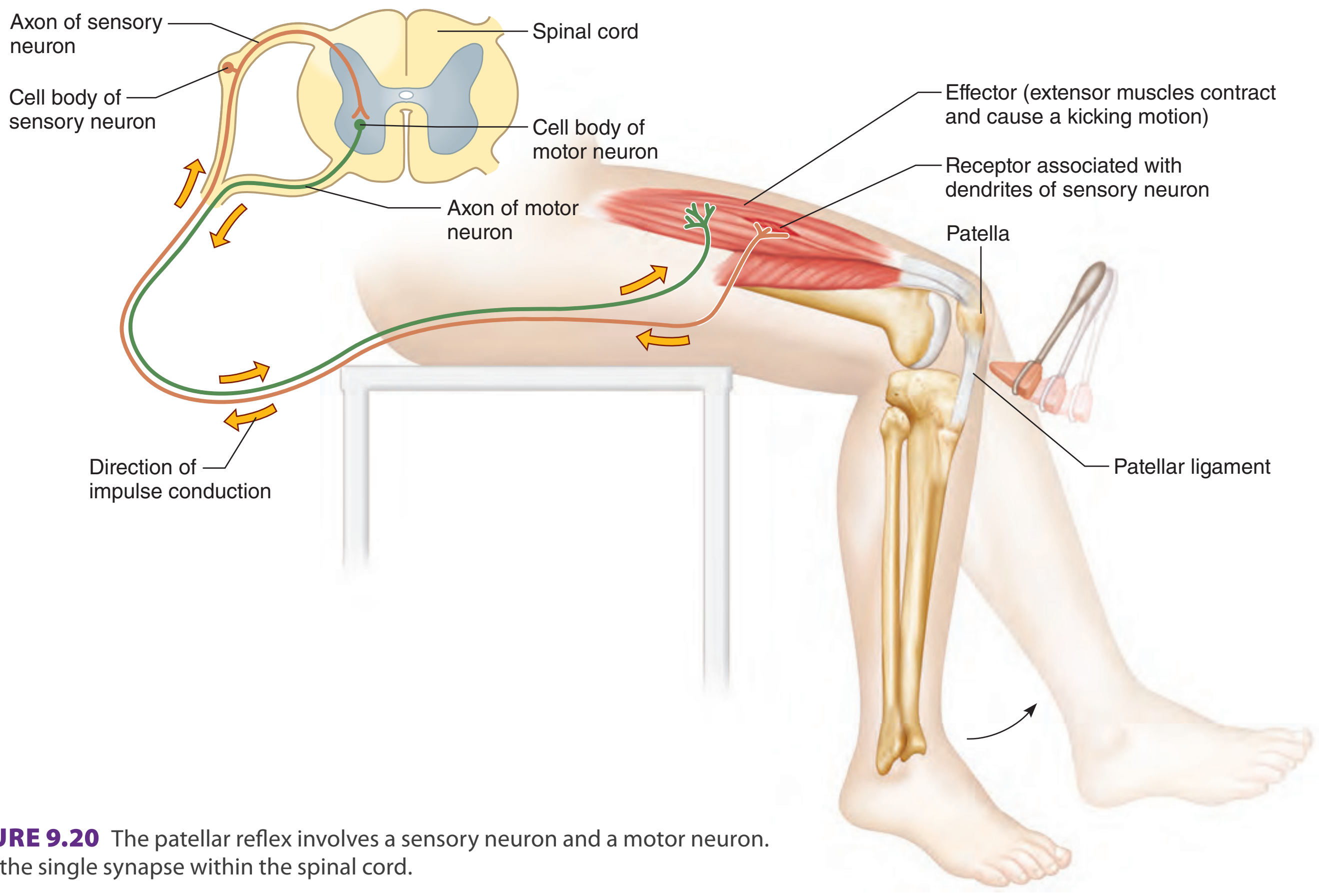

Axon of sensory neuron
Cell body of sensory neuron
Spinal cord
Cell body of motor neuron
Axon of motor neuron
Effector (extensor muscles contract and cause a kicking motion)
Receptor associated with dendrites of sensory neuron
Patella
Patellar ligament
Direction of impulse conduction

**FIGURE 9.20** The patellar reflex involves a sensory neuron and a motor neuron. Note the single synapse within the spinal cord.

Another type of reflex, called a *withdrawal reflex,* occurs when a person unexpectedly touches a body part to something painful, such as stepping on a tack. This activates skin receptors and sends sensory impulses to the spinal cord. There, the impulses pass to the interneurons of a reflex center and are directed to motor neurons. The motor neurons activate fibers in the flexor muscles of the leg and thigh, which contract in response, pulling the foot away from the painful stimulus. At the same time, the antagonistic extensor muscles are inhibited. This inhibition of antagonists allows the flexor muscles to effectively withdraw the affected part. Concurrent with the withdrawal reflex, other interneurons carry sensory impulses to the brain and the person becomes aware of the experience and may feel pain (fig. 9.21). A withdrawal reflex is protective because it may limit tissue damage caused by touching something harmful. Table 9.4 summarizes the parts of a reflex arc.

Reflexes provide information about the condition of the nervous system. An anesthesiologist may try to initiate a reflex in a patient being anesthetized to determine how well the anesthetic drug is affecting nerve functions. A neurologist may test reflexes to determine the location and extent of damage from a nervous system injury.

## PRACTICE

27. What is a nerve pathway?
28. List the parts of a reflex arc.
29. Define *reflex*.
30. List the actions that occur during a withdrawal reflex.

## 9.12 | Meninges

Bones, membranes, and fluid surround the organs of the CNS. The brain lies in the cranial cavity of the skull, and the spinal cord occupies the vertebral canal in the vertebral column. Layered membranes called **meninges** (mĕ-nin′jēz) (singular, *meninx*) lie between these bony coverings and the soft tissues of the CNS, protecting the brain and spinal cord (fig. 9.22*a*).

The meninges have three layers—dura mater, arachnoid mater, and pia mater (fig. 9.22*b*). The **dura mater** (du′rah ma′ter) is the outermost layer. It is composed primarily of tough, white, fibrous connective tissue and contains many blood vessels and nerves. It attaches to the inside of the cranial cavity and forms the internal periosteum of the surrounding skull bones. In some regions, the dura mater extends inward between

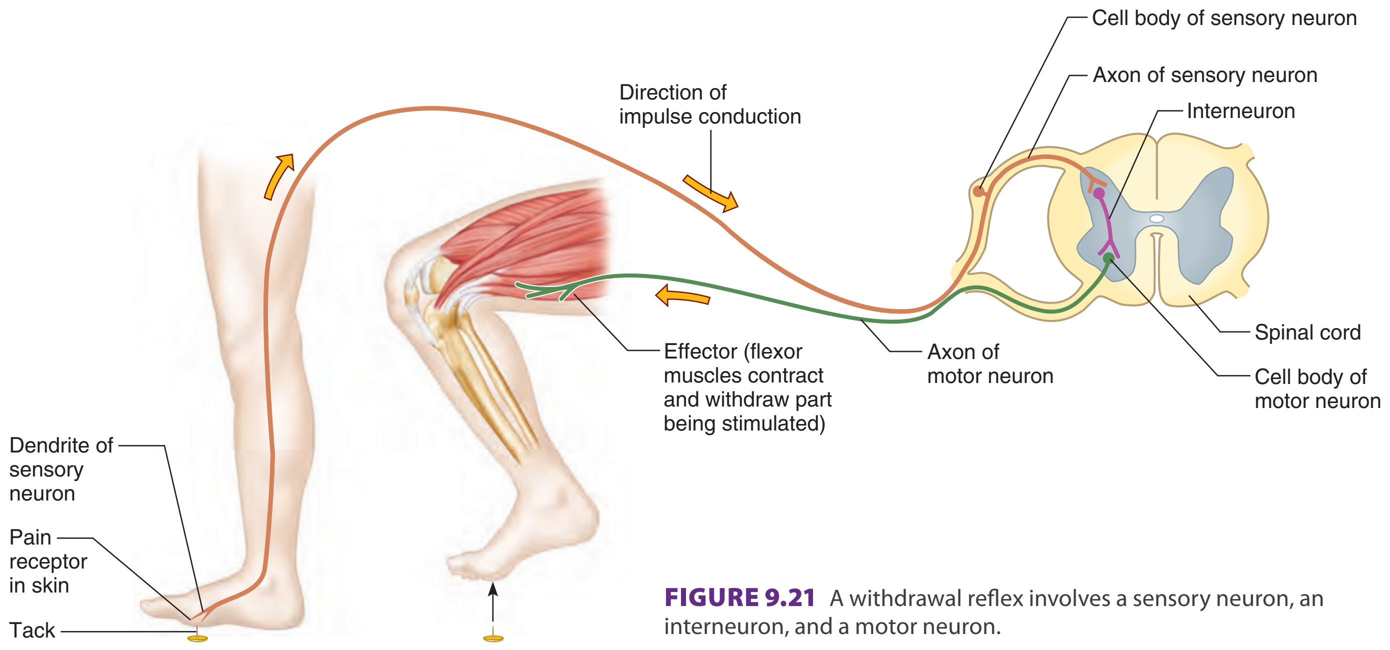

Cell body of sensory neuron
Axon of sensory neuron
Interneuron
Direction of impulse conduction
Spinal cord
Cell body of motor neuron
Effector (flexor muscles contract and withdraw part being stimulated)
Axon of motor neuron
Dendrite of sensory neuron
Pain receptor in skin
Tack

**FIGURE 9.21** A withdrawal reflex involves a sensory neuron, an interneuron, and a motor neuron.

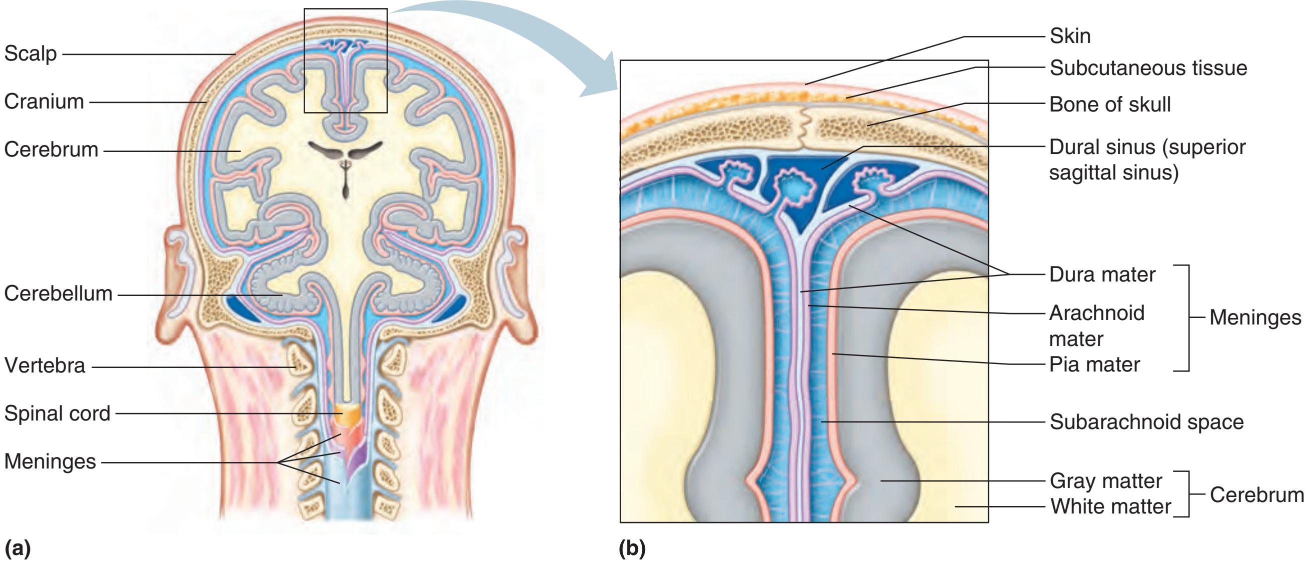

Scalp
Cranium
Cerebrum
Cerebellum
Vertebra
Spinal cord
Meninges
(a)
Skin
Subcutaneous tissue
Bone of skull
Dural sinus (superior sagittal sinus)
Dura mater
Arachnoid mater
Pia mater
Meninges
Subarachnoid space
Gray matter
White matter
Cerebrum
(b)

**FIGURE 9.22** APR Meninges. **(a)** Membranes called meninges enclose the brain and spinal cord. **(b)** The meninges include three layers: dura mater, arachnoid mater, and pia mater.

lobes of the brain and forms partitions that support and protect these parts.

The dura mater continues into the vertebral canal as a strong, tubular sheath that surrounds the spinal cord. It terminates as a blind sac below the end of the cord. The membrane around the spinal cord is not attached directly to the vertebrae but is separated by an *epidural space,* which lies between the dural sheath and the bony walls (fig. 9.23). This space contains loose connective and adipose tissues, which pad the spinal cord.

The **arachnoid mater** is a thin, weblike membrane without blood vessels that lies between the dura and pia maters. A *subarachnoid space* contains the clear, watery **cerebrospinal fluid (CSF).** The **pia mater** (pi′ah ma′ter) is very thin and contains many nerves and blood vessels that nourish underlying cells of the brain and spinal cord. This layer hugs the surfaces of these organs and follows their irregular contours, passing over high areas and dipping into depressions.

## TABLE 9.4 Parts of a Reflex Arc

| Part | Description | Function |
|---|---|---|
| Receptor | Receptor end of a dendrite or a specialized receptor cell in a sensory organ | Senses specific type of internal or external change |
| Sensory neuron | Dendrite, cell body, and axon of a sensory neuron | Carries information from receptor into brain or spinal cord |
| Interneuron | Dendrite, cell body, and axon of a neuron within the brain or spinal cord | Carries information from sensory neuron to motor neuron |
| Motor neuron | Dendrite, cell body, and axon of a motor neuron | Carries instructions from brain or spinal cord out to effector |
| Effector | Muscle or gland | Responds to stimulation by motor neuron and produces reflex or behavioral action |

A blow to the head may break some blood vessels associated with the brain, and escaping blood may collect beneath the dura mater. Such a *subdural hematoma* increases pressure between the rigid bones of the skull and the soft tissues of the brain. Unless the accumulating blood is evacuated, compression of the brain may lead to functional losses or even death.

**PRACTICE**

31. Describe the meninges.
32. State the location of cerebrospinal fluid.

## 9.13 | Spinal Cord

The **spinal cord** is a slender nerve column that passes downward from the brain into the vertebral canal. Although continuous with the brain, the spinal cord begins where nervous tissue leaves the cranial cavity at the level of the foramen magnum. The spinal cord tapers to a point and terminates near the intervertebral disc that separates the first and second lumbar vertebrae (fig. 9.24).

### Structure of the Spinal Cord

The spinal cord consists of thirty-one segments, each of which gives rise to a pair of **spinal nerves.** These nerves (part of the peripheral nervous system) branch

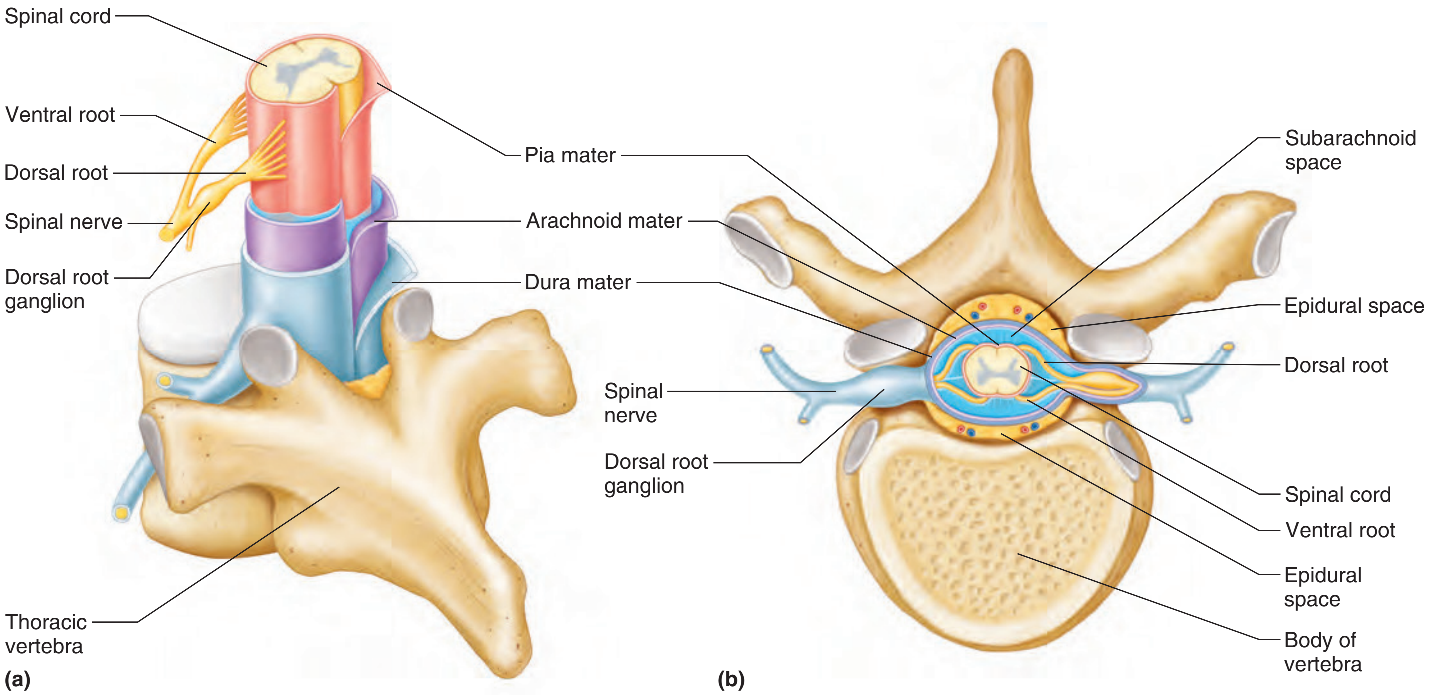

Spinal cord
Ventral root
Dorsal root
Spinal nerve
Dorsal root ganglion
Pia mater
Arachnoid mater
Dura mater
Thoracic vertebra
(a)
Spinal nerve
Dorsal root ganglion
(b)
Subarachnoid space
Epidural space
Dorsal root
Spinal cord
Ventral root
Epidural space
Body of vertebra

**FIGURE 9.23** APR Meninges of the spinal cord. **(a)** The dura mater ensheaths the spinal cord. **(b)** Tissues forming a protective pad around the cord fill the epidural space between the dural sheath and the bone of the vertebra.

to various body parts and connect them with the CNS (see fig. 9.36).

In the neck region, a thickening in the spinal cord, called the *cervical enlargement,* supplies nerves to the upper limbs. A similar thickening in the lower back, the *lumbar enlargement,* gives off nerves to the lower limbs (fig. 9.24).

Two grooves, a deep *anterior median fissure* and a shallow *posterior median sulcus,* extend the length of the spinal cord, dividing it into right and left halves (fig. 9.25). A cross section of the cord reveals a core of gray matter within white matter. The pattern of gray matter roughly resembles a butterfly with its wings spread. The posterior and anterior wings of gray matter are called the *posterior horns* and *anterior horns,* respectively. Between them on either side in the thoracic and upper lumbar segments is a protrusion of gray matter called the *lateral horn.*

Neurons with large cell bodies located in the anterior horns give rise to motor fibers that pass out through spinal nerves to skeletal muscles. However, the majority of neurons in the gray matter of the spinal cord are interneurons.

Gray matter divides the white matter of the spinal cord into three regions on each side—the *anterior, lateral,* and *posterior funiculi* (fig. 9.25*a*). Each funiculus consists of longitudinal bundles of myelinated axons that comprise major neural pathways. In the central nervous system, such bundles of axons are called **tracts.**

A horizontal bar of gray matter in the middle of the spinal cord, the *gray commissure,* connects the wings of the gray matter on the right and left sides. This bar surrounds the **central canal,** which contains cerebrospinal fluid.

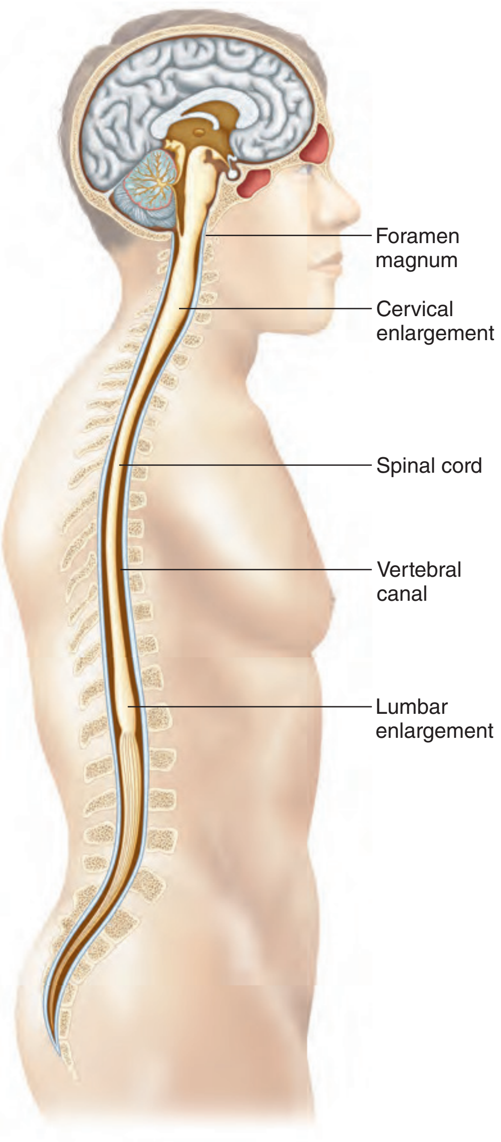


**FIGURE 9.24** APR The spinal cord begins at the level of the foramen magnum and ends near the intervertebral disc between the first and second lumbar vertebrae.

## Functions of the Spinal Cord

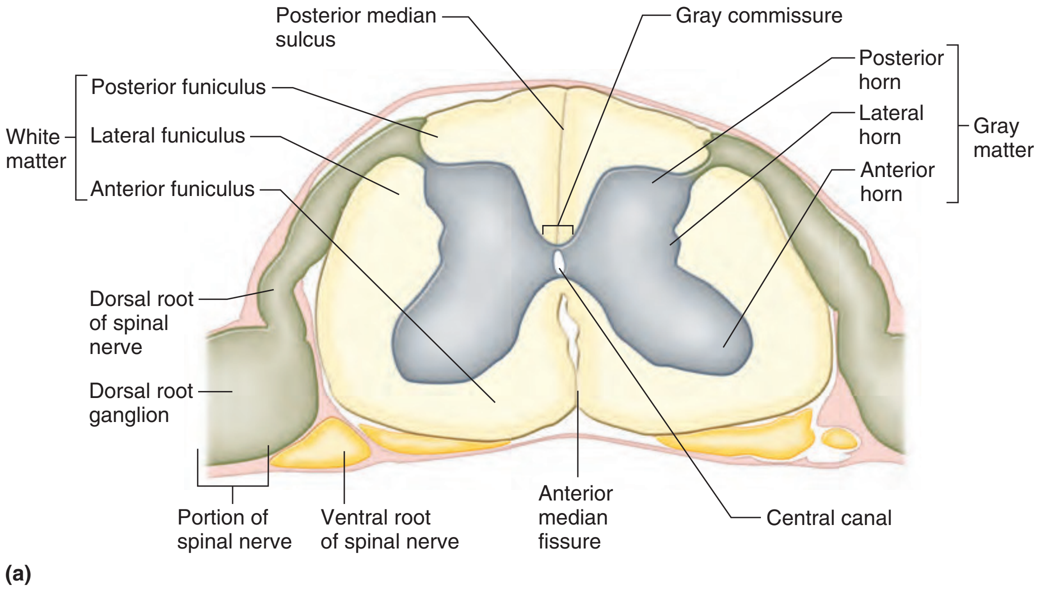
The spinal cord has two major functions—conducting impulses and serving as a center for spinal reflexes. The tracts of the spinal cord consist of axons that provide a two-way communication system between the brain and the body parts outside the nervous system. The tracts that carry sensory information to the brain are called **ascending tracts** (fig. 9.26); those that carry motor instructions from the brain to muscles and glands are called **descending tracts** (fig. 9.27).

All the axons in a given tract typically originate from neuron cell bodies in the same part of the nervous system and terminate together in another part. The names that identify tracts often reflect these common origins and terminations. For example, a *spinothalamic tract* begins in the spinal cord and carries sensory impulses associated with the sensations of pain, touch, and temperature to the thalamus of the brain. A *corticospinal tract* originates in the cortex of the brain and carries motor impulses downward through the spinal cord and spinal nerves. These impulses control skeletal muscle movements.

Corticospinal tracts are also called *pyramidal tracts* after the pyramid-shaped areas in the medulla oblongata of the brain through which they pass. Other descending tracts, called *extrapyramidal tracts,* control motor activities associated with maintaining balance and posture.

In addition to providing a pathway for tracts, the spinal cord functions in many reflexes, including the patellar and withdrawal reflexes described previously. These are called **spinal reflexes** because their reflex arcs pass through the spinal cord.

**FACTS OF LIFE** Some axons extend from the base of the spinal cord to the toes. If you stub your toe, a sensory message reaches the spinal cord in less than one hundredth of a second.


Posterior median sulcus
Gray commissure
Posterior horn
Lateral horn
Anterior horn
Gray matter
White matter
Posterior funiculus
Lateral funiculus
Anterior funiculus
Dorsal root of spinal nerve
Dorsal root ganglion
Portion of spinal nerve
Ventral root of spinal nerve
Anterior median fissure
Central canal
(a)

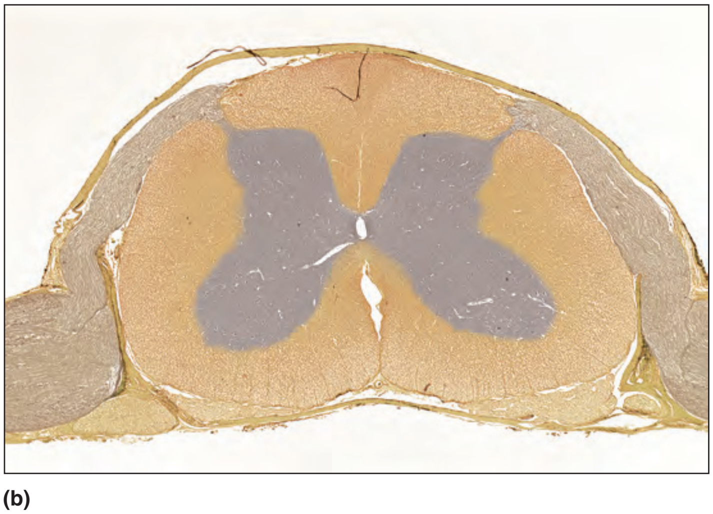


**FIGURE 9.25** APR The spinal cord. **(a)** A cross section of the spinal cord. **(b)** Identify the parts of the spinal cord in this micrograph (10×).

**PRACTICE**

33. Describe the structure of the spinal cord.
34. Describe the general functions of the spinal cord.
35. Distinguish between an ascending and a descending tract.

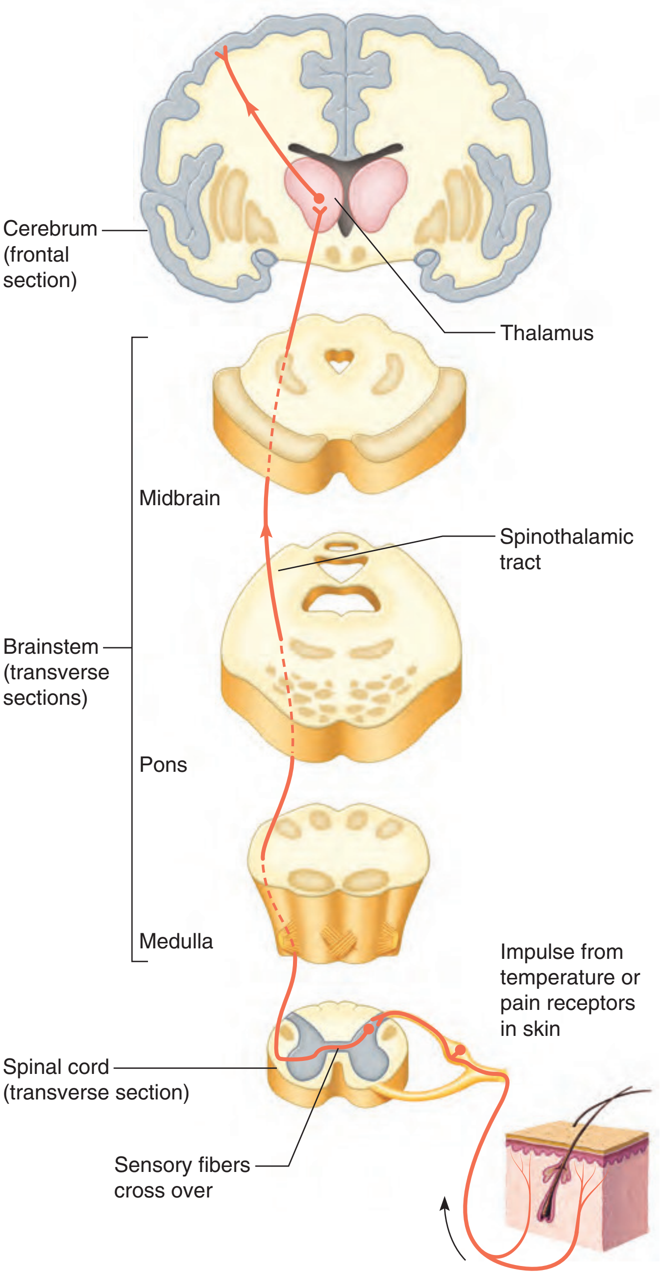
## 9.14 | Brain

The **brain** is composed of about 100 billion ($10^{11}$) multipolar neurons, which communicate with one another and with neurons in other parts of the nervous system. As figure 9.28 shows, the brain can be divided into four major portions—the cerebrum, the diencephalon, the brainstem, and the cerebellum. The *cerebrum,* the largest part, includes nerve centers associated with sensory and motor functions and provides higher mental functions, including memory and reasoning. The *diencephalon* also processes sensory information. Nerve pathways in the *brainstem* connect parts of the nervous system and regulate certain visceral activities. The *cerebellum* includes centers that coordinate voluntary muscular movements.

### Structure of the Cerebrum

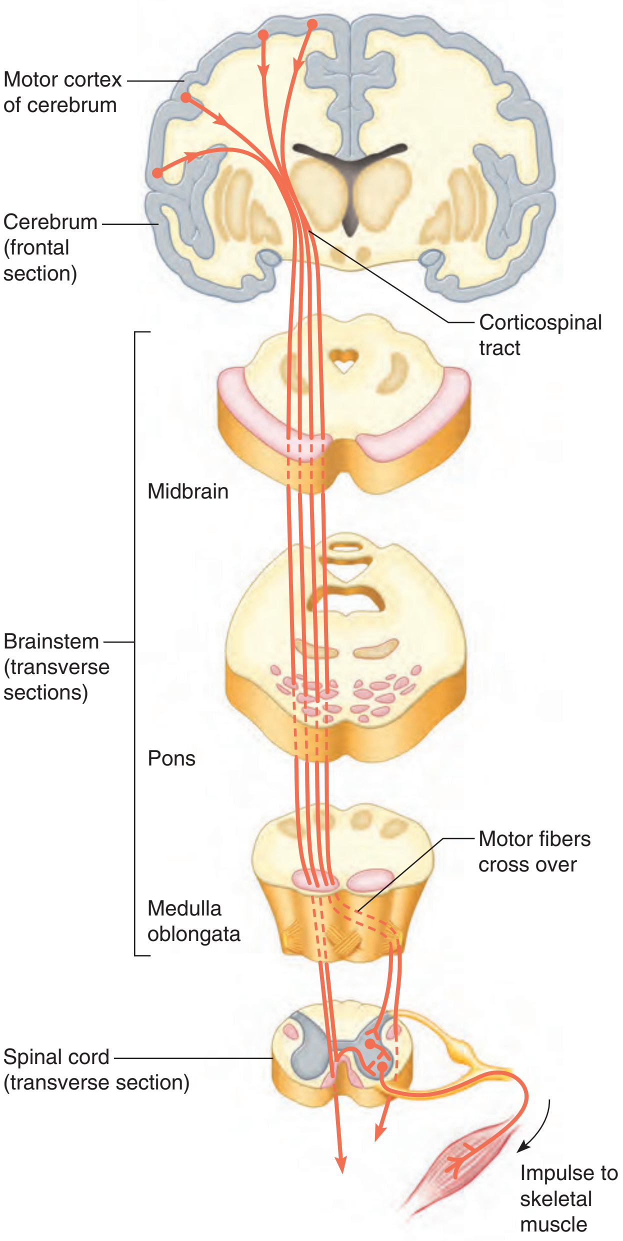
The **cerebrum** (ser′ĕ-brum) consists of two large masses called the left and right **cerebral hemispheres** (ser″ĕ-bral hem′ĭ-sfērz), which are essentially mirror images of each other. A broad, flat bundle of axons called the **corpus callosum** (kor′pus kah-lo′sum) connects the cerebral hemispheres. A layer of dura mater (falx cerebri) separates them.

The surface of the cerebrum has many ridges (convolutions) or **gyri** (ji′ri) (singular, *gyrus*), separated by grooves. A shallow groove is called a **sulcus** (sul′kus), and a deep groove is called a **fissure.** The structural organization of these elevations and depressions is



Cerebrum (frontal section)
Thalamus
Midbrain
Spinothalamic tract
Brainstem (transverse sections)
Pons
Medulla
Impulse from temperature or pain receptors in skin
Spinal cord (transverse section)
Sensory fibers cross over

**FIGURE 9.26** Ascending tracts. Sensory impulses originating in skin receptors cross over in the spinal cord and ascend to the brain. Other sensory tracts cross over in the medulla oblongata.



Motor cortex of cerebrum
Cerebrum (frontal section)
Corticospinal tract
Midbrain
Brainstem (transverse sections)
Pons
Motor fibers cross over
Medulla oblongata
Spinal cord (transverse section)
Impulse to skeletal muscle

**FIGURE 9.27** Descending tracts. Motor fibers of the corticospinal tract begin in the cerebral cortex, cross over in the medulla oblongata, and descend in the spinal cord. There, they synapse with neurons whose fibers lead to the spinal nerves that supply skeletal muscles.

complex, but they form distinct patterns in all normal brains. For example, a *longitudinal fissure* separates the right and left cerebral hemispheres, a *transverse fissure* separates the cerebrum from the cerebellum, and several sulci divide each hemisphere into lobes.

The lobes of the cerebral hemispheres are named after the skull bones they underlie (fig. 9.29). They include:

1. **Frontal lobe** The frontal lobe forms the anterior part of each cerebral hemisphere. It is bordered posteriorly by a *central sulcus,* which extends from the longitudinal fissure at a right angle, and inferiorly by a *lateral sulcus,* which extends from the undersurface of the brain along its sides.
2. **Parietal lobe** The parietal lobe is posterior to the frontal lobe and separated from it by the central sulcus.
3. **Temporal lobe** The temporal lobe lies below the frontal and parietal lobes and is separated from them by the lateral sulcus.
4. **Occipital lobe** The occipital lobe forms the posterior part of each cerebral hemisphere and

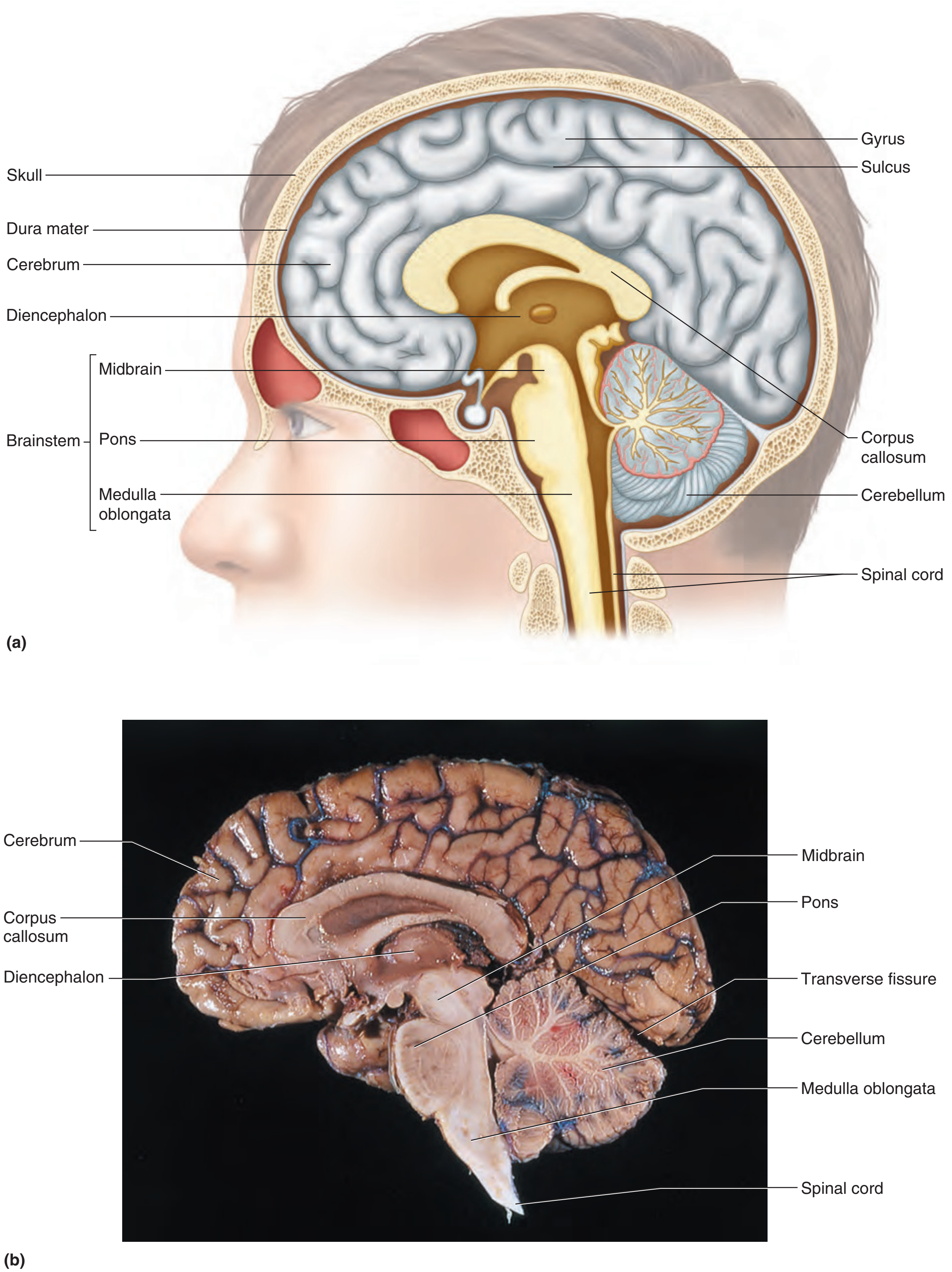

Skull
Dura mater
Cerebrum
Diencephalon
Brainstem
Midbrain
Pons
Medulla oblongata
Gyrus
Sulcus
Corpus callosum
Cerebellum
Spinal cord
(a)
Cerebrum
Corpus callosum
Diencephalon
Midbrain
Pons
Transverse fissure
Cerebellum
Medulla oblongata
Spinal cord
(b)

**FIGURE 9.28** APR The major portions of the brain are the cerebrum, the diencephalon, the brainstem, and the cerebellum. (**a** and **b**)

is separated from the cerebellum by a shelflike extension of dura mater (tentorium cerebelli). The boundary between the occipital lobe and the parietal and temporal lobes is not distinct.

5. **Insula** (in′su-lah) The insula is deep in the lateral sulcus and is covered by parts of the frontal, parietal, and temporal lobes. A *circular sulcus* separates the insula from the other lobes.

A thin layer of gray matter called the **cerebral cortex** (ser″ĕ-bral kor′teks) is the outermost part of the cerebrum. This layer covers the gyri and dips into the sulci and fissures. It contains nearly 75% of all the neuron cell bodies in the nervous system.

Just beneath the cerebral cortex is a mass of white matter that makes up the bulk of the cerebrum. This mass contains bundles of myelinated axons that connect neuron cell bodies of the cortex with other parts of the nervous system. Some of these fibers pass from one cerebral hemisphere to the other by way of the corpus callosum, and others carry sensory or motor impulses from parts of the cortex to nerve centers in the brain or spinal cord.

In a condition called lissencephaly, which means "smooth brain," sulci and gyri are absent. Lissencephaly is associated with intellectual disability, developmental delay, and seizures.

## Functions of the Cerebrum

The cerebrum provides higher brain functions. It has centers for interpreting sensory impulses arriving from sense organs and centers for initiating voluntary muscular movements. The cerebrum stores the information that constitutes memory and utilizes it to reason. Intelligence and personality also stem from cerebral activity.

### *Functional Regions of the Cerebral Cortex*

Specific regions of the cerebral cortex perform specific functions. Although functions overlap among regions, the cortex can be divided into sensory, association, and motor areas.

**Sensory areas** in several lobes of the cerebrum interpret impulses that arrive from sensory receptors, producing feelings or sensations. For example, sensations from all parts of the skin (cutaneous senses) arise in the anterior parts of the parietal lobes along the central sulcus (fig. 9.29). The posterior parts of the occipital lobes affect vision (visual area), and the temporal lobes contain the centers for hearing (auditory area). The sensory areas for taste are located near the bases of the central sulci along the lateral sulci, and the sense of smell arises from centers deep within the cerebrum.

Like motor fibers, sensory fibers cross over either in the spinal cord or in the brainstem (see fig. 9.26). Thus, the centers in the right cerebral hemisphere interpret impulses originating from the left side of the body, and vice versa.

Not all sensory areas are bilateral. The *sensory speech area* or *Wernicke's* (ver′nĭ-kēz) *area* is in the temporal lobe, adjacent to the parietal lobe near the posterior end of the lateral sulcus, usually in the left hemisphere. This area receives and relays input from both the visual cortex and auditory cortex and is important for understanding written or spoken language.

**Association areas** are neither primarily sensory nor primarily motor. They connect with one another and with other brain structures. Association areas analyze and interpret sensory experiences and oversee memory, reasoning, verbalizing, judgment, and emotion. Association areas occupy the anterior portions of the frontal lobes and are widespread in the lateral parts of the parietal, temporal, and occipital lobes (fig. 9.29).

The functions of the insula are not as well known as those of the other lobes, because its location deep within the cerebrum makes it impossible to study with surface electrodes. However, studies that use functional MRI scanning suggest that the insula serves as a crossroads for translating sensory information into appropriate emotional responses, such as feeling disgust at the sight of a cat regurgitating a hairball, or a feeling of joy when hearing a symphony or when biting into a slice of pizza. Some researchers hypothesize that the insula is, in some complex way, responsible for some of the qualities that make us human.

The association areas of the frontal lobes control a number of higher intellectual processes. These include concentrating, planning, complex problem solving, and judging the possible consequences of behavior. Association areas of the parietal lobes help in understanding speech and choosing words to express thoughts and feelings.

Wernicke's area corresponds closely to a brain region that has been referred to as a "general interpretive area," near where the occipital, parietal, and temporal lobes meet. It plays a role in integrating visual, auditory, and other sensory information, and then interpretating a situation. For example, you hear a familiar voice, look up from your notes, see a friend from class, and realize that it is time for your study group.

The association areas of the temporal lobes and the regions of the posterior ends of the lateral sulcus store memory of visual scenes, music, and other complex sensory patterns. Association areas of the occipital lobes that are adjacent to the visual centers are important in analyzing visual patterns and combining visual images with other sensory experiences, as when one recognizes another person or an object.

The primary **motor areas** of the cerebral cortex lie in the frontal lobes, just in front of the central sulcus (fig. 9.29). The nervous tissue in these regions contains many large *pyramidal cells,* named for their pyramid-shaped cell bodies. These cells are also termed *upper motor neurons,* because of their location.

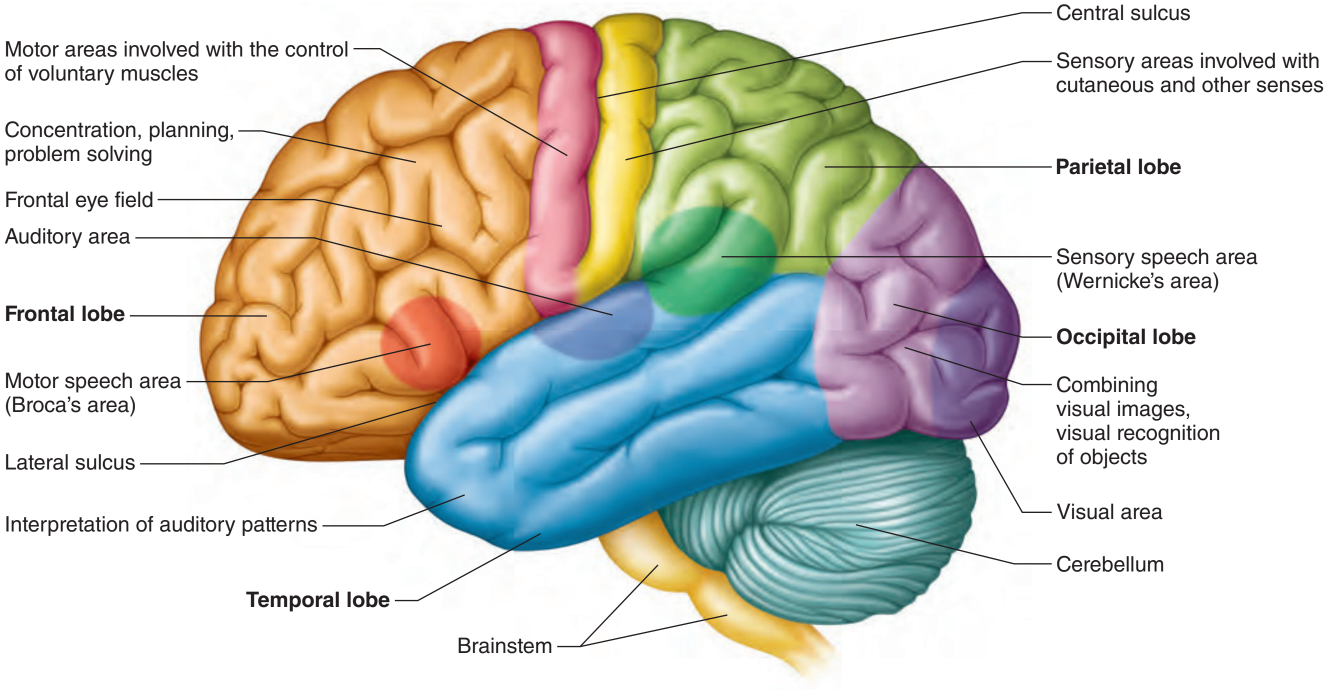

Motor areas involved with the control of voluntary muscles
Concentration, planning, problem solving
Frontal eye field
Auditory area
Frontal lobe
Motor speech area (Broca's area)
Lateral sulcus
Interpretation of auditory patterns
Temporal lobe
Brainstem
Central sulcus
Sensory areas involved with cutaneous and other senses
Parietal lobe
Sensory speech area (Wernicke's area)
Occipital lobe
Combining visual images, visual recognition of objects
Visual area
Cerebellum

**FIGURE 9.29** APR Some sensory, association, and motor areas of the left cerebral cortex.

Impulses from the pyramidal cells travel downward through the brainstem and into the spinal cord on the corticospinal tracts (see fig. 9.27). Here they form synapses with *lower motor neurons* whose axons leave the spinal cord and reach skeletal muscle fibers. Most of the axons in these tracts cross over from one side of the brain to the other within the brainstem. As a result, the motor area of the right cerebral hemisphere generally controls skeletal muscles on the left side of the body, and vice versa.

In addition to the primary motor areas, certain other regions of the frontal lobe affect motor functions. For example, a region called the *motor speech area,* or *Broca's* (bro′kahz) *area,* is usually in the left hemisphere, just anterior to the primary motor cortex and superior to the lateral sulcus. This area generates the movements of muscles necessary for speech (fig. 9.29).

Above the motor speech area is a region called the *frontal eye field.* The motor cortex in this area controls voluntary movements of the eyes and eyelids. Another region just in front of the primary motor area controls the muscular movements of the hands and fingers that make skills such as writing possible.

## PRACTICE

36. List the major divisions of the brain.
37. Describe the cerebral cortex.
38. Describe the major functions of the cerebrum.
39. Locate the major functional regions of the cerebral cortex.

The effects of injuries to the cerebral cortex depend on the location and extent of the damage. For example, injury to the motor areas of one frontal lobe causes partial or complete paralysis on the opposite side of the body. Damage to the association areas of the frontal lobe may impair concentration on complex mental tasks, making a person appear disorganized and easily distracted. Damage to association areas of the temporal lobes may impair recognition of printed words or arranging words into meaningful thoughts.

### *Hemisphere Dominance*

Both cerebral hemispheres participate in basic functions, such as receiving and analyzing sensory impulses, controlling skeletal muscles, and storing memory. However, in most persons, one side of the cerebrum is the **dominant hemisphere,** controlling the ability to use and understand language.

In most people the left hemisphere is dominant for the language-related activities of speech, writing, and reading, and for complex intellectual functions requiring verbal, analytical, and computational skills. In other persons, the right hemisphere is dominant for language-related abilities, or the hemispheres are equally dominant. Broca's area in the dominant hemisphere controls the muscles that function in speaking.

In addition to carrying on basic functions, the nondominant hemisphere specializes in nonverbal functions, such as motor tasks that require orientation of the body in space, understanding and interpreting musical patterns, and nonverbal visual experiences. The nondominant hemisphere also controls emotional and intuitive thinking.

Nerve fibers of the corpus callosum, which connect the cerebral hemispheres, allow the dominant hemisphere to control the motor cortex of the nondominant hemisphere (see fig. 9.28). These fibers also transfer sensory information reaching the nondominant hemisphere to the dominant one, where the information can be used in decision making.

Deep within each cerebral hemisphere are several masses of gray matter called **basal nuclei**, also called basal ganglia (fig. 9.30). They are the *caudate nucleus,* the *putamen,* and the *globus pallidus.* The basal nuclei produce the inhibitory neurotransmitter *dopamine.* The neurons of the basal nuclei interact with other brain areas, including the motor cortex, thalamus, and cerebellum. These interactions, through a combination of stimulation and inhibition, facilitate voluntary movement.

The signs of Parkinson disease and Huntington disease result from altered activity of basal nuclei neurons. In Parkinson disease, nearby neurons release less dopamine, and the basal nuclei become overactive, inhibiting movement. In Huntington disease, basal nuclei neurons gradually deteriorate, resulting in unrestrained movement.

## Ventricles and Cerebrospinal Fluid

Interconnected cavities called **ventricles** lie within the cerebral hemispheres and brainstem (fig. 9.31). These spaces are continuous with the central canal of the spinal cord, and like it, they contain cerebrospinal fluid.

The largest ventricles are the *lateral ventricles* (first and second ventricles), which extend into the cerebral hemispheres and occupy parts of the frontal, temporal, and occipital lobes. A narrow space that constitutes the *third ventricle* is in the midline of the brain, beneath the corpus callosum. This ventricle communicates with the lateral ventricles through openings (interventricular foramina) in its anterior end. The *fourth ventricle* is in the brainstem just anterior to the cerebellum. A narrow canal, the *cerebral aqueduct,* connects it to the third ventricle and passes lengthwise through the brainstem. The fourth ventricle is continuous with the central canal of the spinal cord and has openings in its roof that lead into the subarachnoid space of the meninges.

Tiny, reddish, cauliflower-like masses of specialized capillaries from the pia mater, called **choroid plexuses** (plek′sus-ez), secrete cerebrospinal fluid (fig. 9.32). These structures project into the ventricles. Most of the cerebrospinal fluid is formed in the lateral ventricles. From there, it circulates slowly into the third and fourth ventricles and into the central canal of the spinal cord. Cerebrospinal fluid also enters the subarachnoid space of the meninges through the wall of the fourth ventricle near the cerebellum and completes its circuit by being reabsorbed into the blood.

Cerebrospinal fluid completely surrounds the brain and spinal cord because it occupies the subarachnoid space of the meninges. In effect, these organs float in the fluid, which supports and protects them by absorbing forces that might otherwise jar and damage them. Cerebrospinal fluid also maintains a stable ionic concentration in the CNS and provides a pathway to the blood for wastes.

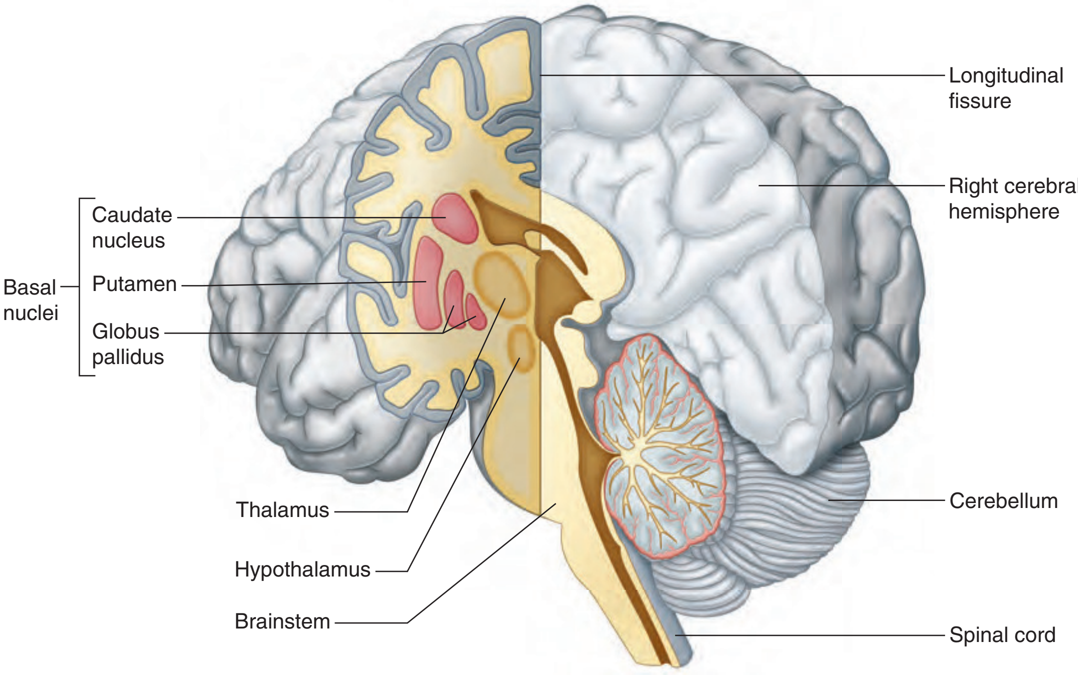
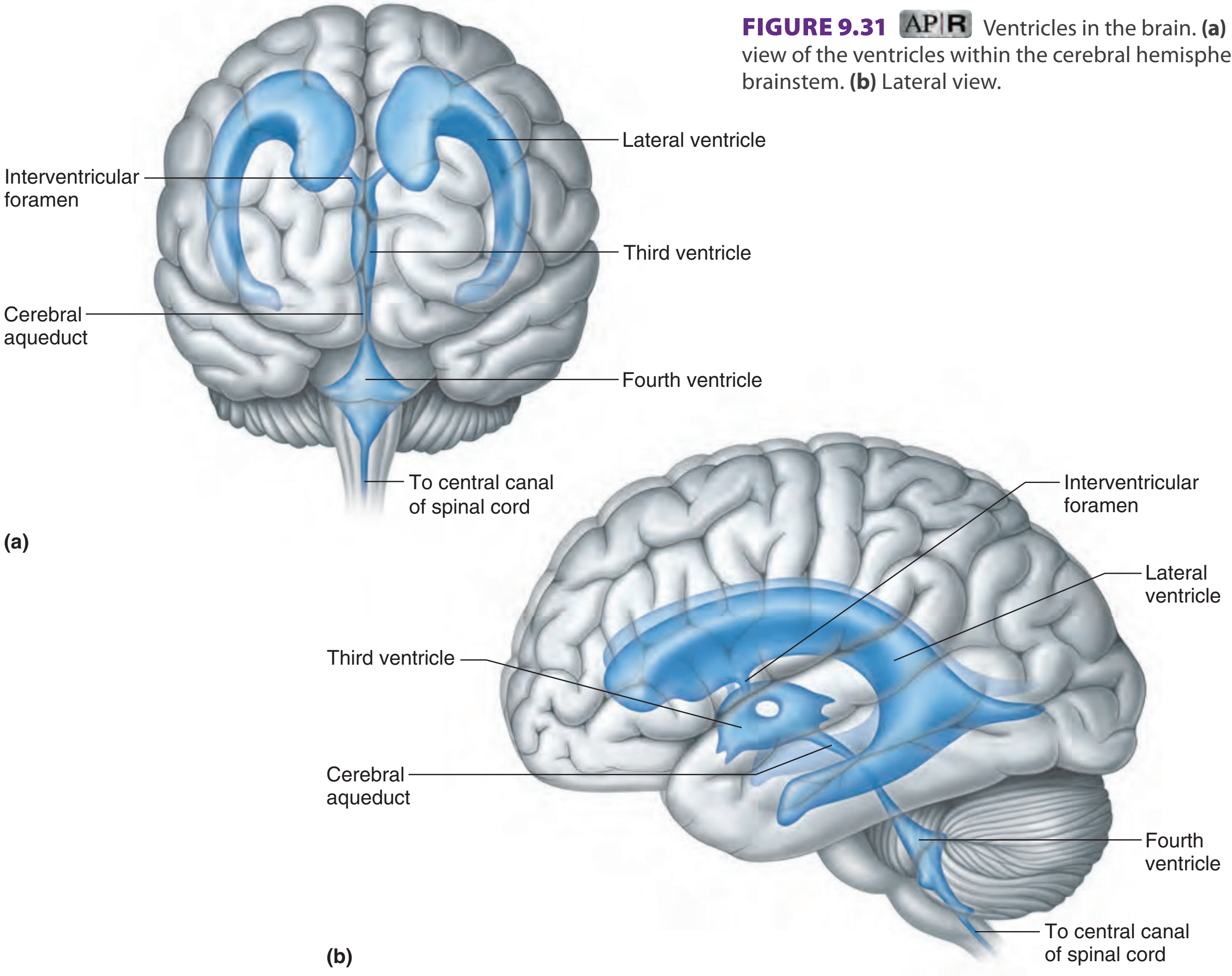


**FIGURE 9.30** APR A frontal (coronal) section of the left cerebral hemisphere (posterior view) reveals some of the basal nuclei.

**FIGURE 9.31** APR Ventricles in the brain. **(a)** Anterior view of the ventricles within the cerebral hemispheres and brainstem. **(b)** Lateral view.


Interventricular foramen
Lateral ventricle
Third ventricle
Cerebral aqueduct
Fourth ventricle
To central canal of spinal cord
(a)
Interventricular foramen
Lateral ventricle
Third ventricle
Cerebral aqueduct
Fourth ventricle
To central canal of spinal cord
(b)

The fluid pressure in the ventricles normally remains relatively constant because cerebrospinal fluid is secreted and reabsorbed continuously and at equal rates. An infection, a tumor, or a blood clot can interfere with fluid circulation, increasing pressure in the ventricles and thus in the cranial cavity (intracranial pressure). This can injure the brain by forcing it against the rigid skull.

A *lumbar puncture* (spinal tap) measures the pressure of cerebrospinal fluid. A very thin hollow needle is inserted into the subarachnoid space between the third and fourth or between the fourth and fifth lumbar vertebrae and an instrument called a *manometer* measures the pressure.

**PRACTICE**

40. What is hemisphere dominance?
41. What are the major functions of the dominant hemisphere? The nondominant one?
42. Where are the ventricles of the brain?
43. Describe the circulation of cerebrospinal fluid.

## Diencephalon

The **diencephalon** (di″en-sef′ah-lon) is located between the cerebral hemispheres and above the midbrain. It surrounds the third ventricle and is composed largely of gray matter. Within the diencephalon, a dense mass called the **thalamus** bulges into the third ventricle from each side (see figs. 9.30 and 9.33*b*). Another region of the diencephalon that includes many nuclei (masses of gray matter) is the **hypothalamus.** It lies below the thalamus and forms the lower walls and floor of the third ventricle.

The thalamus is a central relay station for sensory impulses ascending from other parts of the nervous system to the cerebral cortex. It receives all sensory impulses (except those associated with the sense of smell) and channels them to the appropriate regions of the cortex for interpretation. In addition, all regions of the cerebral cortex can communicate with the thalamus by means of descending fibers. The cerebral cortex pinpoints the origin of sensory stimulation, and the thalamus produces a general awareness of certain sensations, such as pain, touch, and temperature.

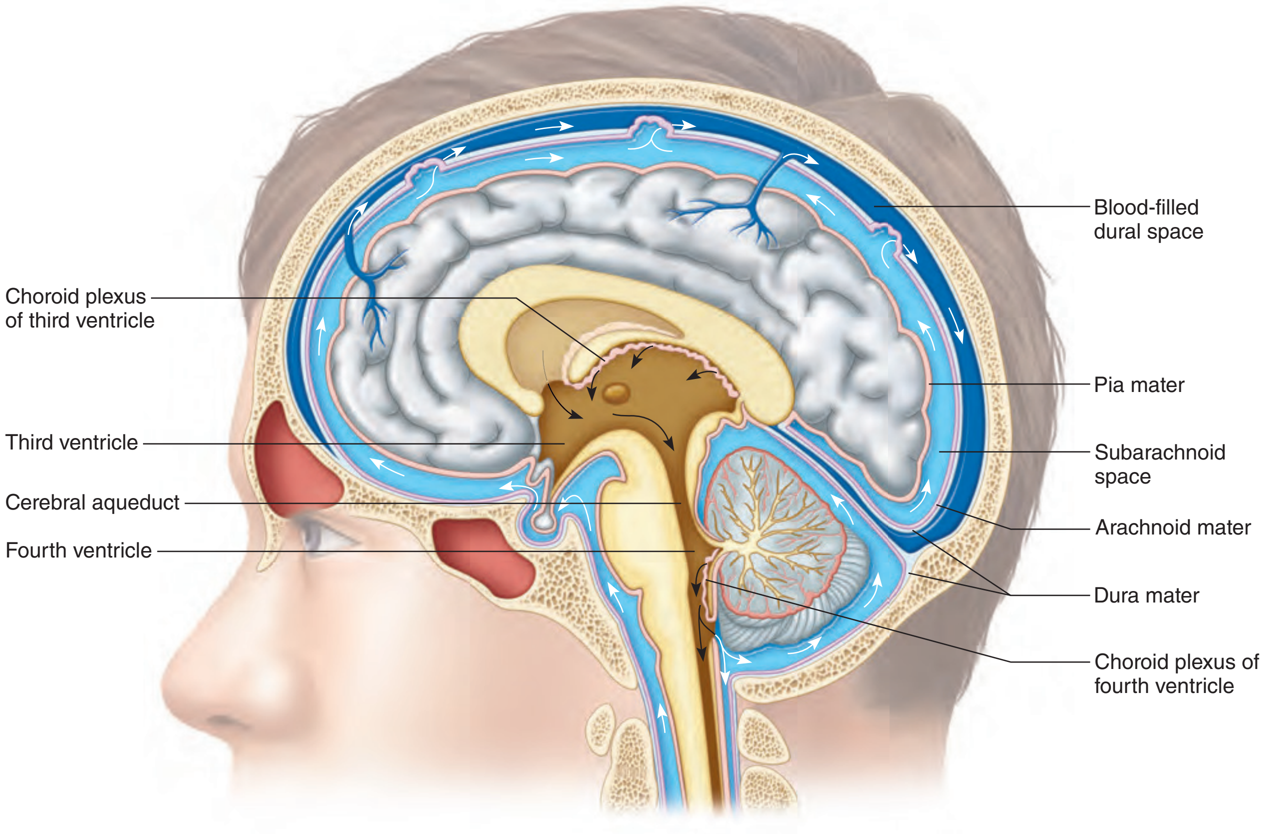


**FIGURE 9.32** APR The choroid plexuses in the walls of the ventricles secrete cerebrospinal fluid. The fluid circulates through the ventricles and central canal, enters the subarachnoid space, and is reabsorbed into the blood.

Nerve fibers connect the hypothalamus to the cerebral cortex, thalamus, and other parts of the brainstem. The hypothalamus maintains homeostasis by regulating a variety of visceral activities and by linking the nervous and endocrine systems. The hypothalamus regulates:

1. Heart rate and arterial blood pressure
2. Body temperature
3. Water and electrolyte balance
4. Control of hunger and body weight
5. Control of movements and glandular secretions of the stomach and intestines
6. Production of neurosecretory substances that stimulate the pituitary gland to secrete hormones
7. Sleep and wakefulness

Structures in the general region of the diencephalon also control emotional responses. For example, regions of the cerebral cortex in the medial parts of the frontal and temporal lobes interconnect with a number of deep masses of gray matter, including the hypothalamus, thalamus, and basal nuclei. Together, these structures compose a complex called the **limbic system.**

The limbic system controls emotional experience and expression. It can modify the way a person acts by producing such feelings as fear, anger, pleasure, and sorrow. The limbic system recognizes upsets in a person's physical or psychological condition that might threaten life. By causing pleasant or unpleasant feelings about experiences, the limbic system guides a person into behavior that is likely to increase the chance of survival.

A whiff of a certain scent may elicit vivid memories because sensory information from olfactory receptors (the sense of smell) also goes to the limbic system. Olfactory input to the limbic system is also why odors can alter mood. For example, the scent of just-mowed grass or an ocean breeze makes us feel good.

Other parts of the diencephalon include: (1) the **optic tracts** and the **optic chiasma** that is formed by optic nerve fibers crossing over each other; (2) the **infundibulum,** a conical process behind the optic chiasma to which the pituitary gland attaches; (3) the **posterior pituitary gland,** which hangs from the floor of the hypothalamus; (4) the **mammillary bodies,** which appear as two rounded structures behind the infundibulum; and (5) the **pineal gland** (pin′e-al gland), a cone-shaped structure attached to the upper part of the diencephalon (see chapter 11, p. 320).

## Brainstem

The **brainstem** is a bundle of nervous tissue that connects the cerebrum to the spinal cord. It consists of many tracts and several nuclei. The parts of the brainstem include the midbrain, pons, and medulla oblongata (figs. 9.28 and 9.33).

### *Midbrain*

The **midbrain** is a short section of the brainstem between the diencephalon and the pons (see fig. 9.28). It contains bundles of myelinated axons that join lower parts of the brainstem and spinal cord with higher parts of the brain. Two prominent bundles of axons on the underside of the midbrain are the corticospinal tracts and are the main motor pathways between the cerebrum and lower parts of the nervous system.

The midbrain includes several masses of gray matter that serve as reflex centers. For example, the midbrain contains the centers for certain visual reflexes, such as those responsible for moving the eyes to view something as the head turns. It also contains the auditory reflex centers that enable a person to move the head to hear sounds more distinctly.

### *Pons*

The **pons** (ponz) is a rounded bulge on the underside of the brainstem, where it separates the midbrain from the medulla oblongata (see fig. 9.28). The dorsal part of the pons consists largely of longitudinal nerve fibers, which relay impulses to and from the medulla oblongata and the cerebrum. The ventral part of the pons has large bundles of transverse nerve fibers, which transmit impulses from the cerebrum to centers in the cerebellum.

Several nuclei of the pons relay sensory impulses from peripheral nerves to higher brain centers. Other nuclei may contribute to the rhythm of breathing (see chapter 16, p. 469).

### *Medulla Oblongata*

The **medulla oblongata** (mĕ-dul′ah ob″long-gah′tah) extends from the pons to the foramen magnum of the skull (see fig. 9.28). Its dorsal surface flattens to form the floor of the fourth ventricle, and its ventral surface is marked by the corticospinal tracts, most of whose fibers cross over at this level (see fig. 9.27).

All of the ascending and descending nerve fibers connecting the brain and spinal cord must pass through the medulla oblongata because of its location. In the spinal cord the white matter surrounds a central mass of gray matter. Here in the medulla oblongata, however, nerve fibers separate the gray matter into nuclei, some of which relay ascending impulses to the other side of the brainstem and then on to higher brain centers. Other nuclei in the medulla oblongata control vital visceral activities. These centers include:

1. **Cardiac center** Impulses originating in the cardiac center are transmitted to the heart on peripheral nerves, altering heart rate.
2. **Vasomotor center** Certain cells of the vasomotor center initiate impulses that travel to smooth muscle in the walls of certain blood vessels and stimulate the smooth muscle to contract. This constricts the blood vessels (vasoconstriction), maintaining blood pressure. Other cells of the vasomotor center produce the opposite effect—dilating blood vessels (vasodilation) and consequently dropping blood pressure.
3. **Respiratory center** The respiratory center maintains breathing rhythm and adjusts the rate and depth of breathing.

Still other nuclei in the medulla oblongata are centers for the reflexes associated with coughing, sneezing, swallowing, and vomiting.

### *Reticular Formation*

Scattered throughout the medulla oblongata, pons, and midbrain is a complex network of nerve fibers associated with tiny islands of gray matter. This network, the **reticular formation** (rĕ-tik′u-lar for-ma′shun), also called the reticular activating system, extends from the upper part of the spinal cord into the diencephalon. Its nerve fibers join centers of the hypothalamus, basal nuclei, cerebellum, and cerebrum with fibers in all the major ascending and descending tracts.

When sensory impulses reach the reticular formation, it responds by activating the cerebral cortex into a state of wakefulness. Without this arousal, the cortex remains unaware of stimulation and cannot interpret sensory information or carry on thought processes. Thus, decreased activity in the reticular formation results in sleep. If the reticular formation is injured so that it cannot function, the person remains unconscious and cannot be aroused, even with strong stimulation. This is called a comatose state. Barbiturate drugs, which dampen CNS activity, affect the reticular formation (see Clinical Application 9.2).

**PRACTICE**

44. What are the major functions of the thalamus? The hypothalamus?
45. How may the limbic system influence behavior?
46. List the structures of the brainstem.
47. Which vital reflex centers are in the brainstem?
48. What is the function of the reticular formation?

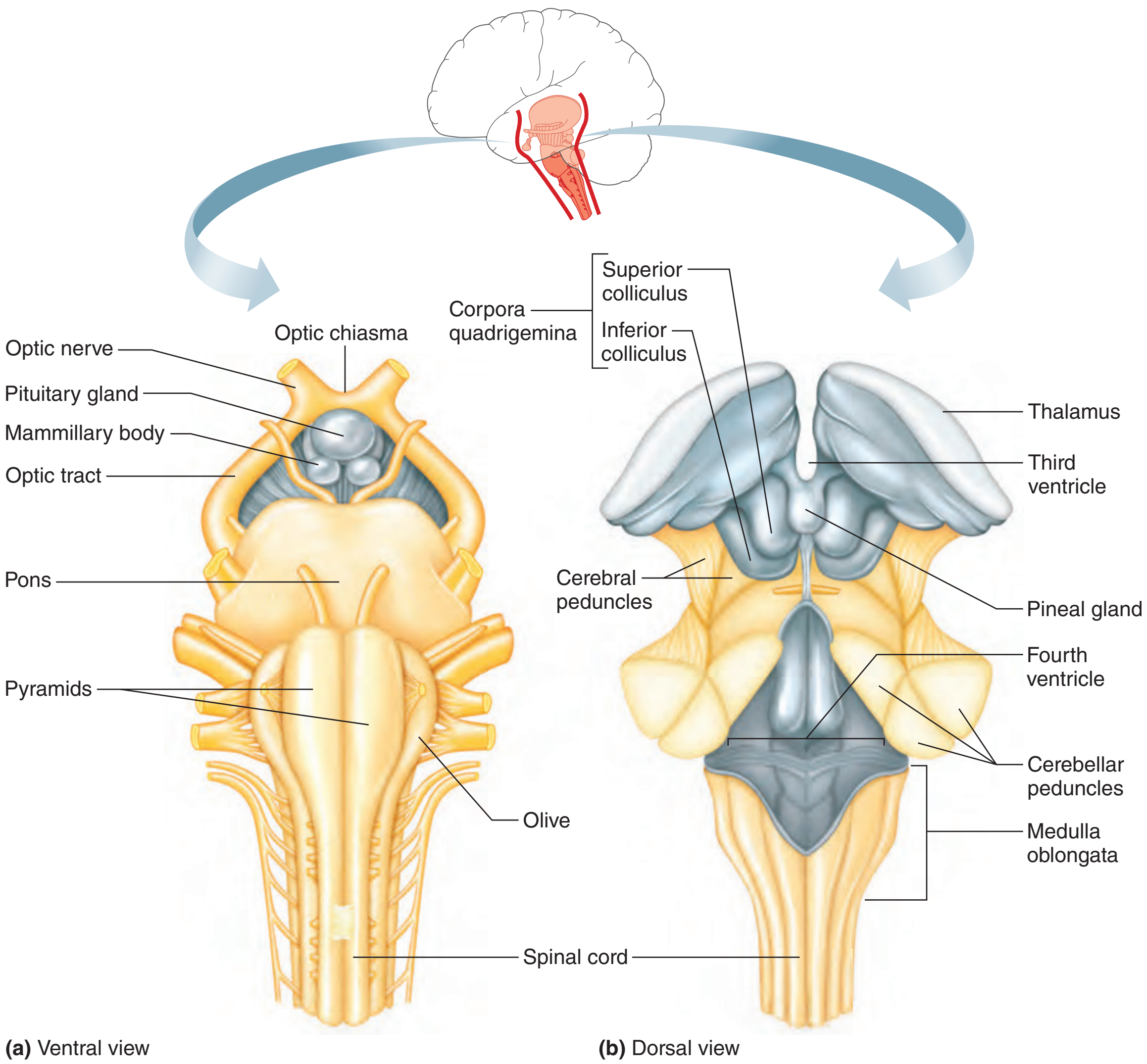

Optic nerve
Optic chiasma
Pituitary gland
Mammillary body
Optic tract
Pons
Pyramids
Olive
Spinal cord
Corpora quadrigemina
Superior colliculus
Inferior colliculus
Thalamus
Third ventricle
Cerebral peduncles
Pineal gland
Fourth ventricle
Cerebellar peduncles
Medulla oblongata
(a) Ventral view
(b) Dorsal view

**FIGURE 9.33** APR The brainstem. **(a)** Ventral view of the brainstem. **(b)** Dorsal view of the brainstem with the cerebellum removed, exposing the fourth ventricle.

Q *What is the relative position of the fourth ventricle to the third ventricle?*
**Answer can be found in Appendix F on page 582.**

## Cerebellum

The **cerebellum** (ser″ĕ-bel′um) is a large mass of tissue located below the occipital lobes of the cerebrum and posterior to the pons and medulla oblongata (see fig. 9.28). It consists of two lateral hemispheres partially separated by a layer of dura mater (falx cerebelli) and connected in the midline by a structure called the *vermis.* Like the cerebrum, the cerebellum is composed primarily of white matter, with a thin layer of gray matter, the **cerebellar cortex,** on its surface.

The cerebellum communicates with other parts of the CNS by means of three pairs of nerve tracts called *cerebellar peduncles* (figs. 9.33 and 9.34). One pair (the inferior peduncles) brings sensory information concerning the position of the limbs, joints, and other body parts to the cerebellum. Another pair (the middle peduncles) transmits signals from the cerebral cortex to the cerebellum concerning the desired positions of these parts. After integrating and analyzing this information, the cerebellum sends correcting impulses via a third pair (the superior peduncles) to the midbrain. These corrections are incorporated into motor impulses that travel downward through the pons, medulla oblongata, and spinal cord in the appropriate patterns to move the body in the desired way.

The cerebellum is a reflex center for integrating sensory information concerning the position of body parts and for coordinating complex skeletal muscle movements. It also helps maintain posture. Damage to the cerebellum is likely to result in tremors, inaccurate movements of voluntary muscles, loss of muscle tone, a reeling walk, and loss of equilibrium.

## CLINICAL APPLICATION 9.2

## Drug Abuse

*Drug abuse* is the chronic self-administration of a drug in doses high enough to cause *addiction*—a physical or psychological dependence in which the user is preoccupied with locating and taking the drug. Stopping drug use causes intense, unpleasant withdrawal symptoms. Prolonged and repeated abuse of a drug may also result in *drug tolerance,* in which the physiological response to a particular dose of the drug becomes less intense over time. Drug tolerance results as the drug increases synthesis of certain liver enzymes, which metabolize the drug more rapidly, so that the addict needs the next dose sooner. Drug tolerance also arises from physiological changes that lessen the drug's effect on its target cells. The most commonly abused drugs are CNS depressants ("downers"), CNS stimulants ("uppers"), hallucinogens, and anabolic steroids (see Clinical Application 8.1, p. 198).

**CNS depressants** include barbiturates, benzodiazepines, opiates, and cannabinoids. *Barbiturates* act uniformly throughout the brain, but the reticular formation is particularly sensitive to their effects. CNS depression occurs due to inhibited secretion of certain excitatory and inhibitory neurotransmitters. Effects range from mild calming of the nervous system (sedation) to sleep, loss of sensory sensations (anesthesia), respiratory distress, cardiovascular collapse, and death.

The *benzodiazepines,* such as diazepam, depress activity in the limbic system and the reticular formation. Low doses relieve anxiety, and higher doses cause sedation, sleep, or anesthesia. These drugs increase either the activity or release of the inhibitory neurotransmitter GABA. When benzodiazepines are metabolized, they may form other biochemicals that have depressing effects.

The *opiates* include heroin (which has no legal use in the United States), codeine, morphine, meperidine, and methadone. These drugs stimulate certain receptors (opioid receptors) in the CNS, and when taken in prescribed dosages, they sedate and relieve pain (analgesia). Opiates cause both physical and psychological dependence. Effects of overdose include a feeling of well-being (euphoria), respiratory distress, convulsions, coma, and possible death. On the other hand, these drugs are very important in treating chronic, severe pain. For example, cancer patients find pain relief with oxycodone, which is taken twice daily in a timed-release pill.

The *cannabinoids* include marijuana and hashish, both derived from the hemp plant. Hashish is several times more potent than marijuana. These drugs depress higher brain centers and release lower brain centers from the normal inhibitory influence of the higher centers. This induces an anxiety-free state, characterized by euphoria and a distorted perception of time and space. *Hallucinations* (sensory perceptions that have no external stimuli), respiratory distress, and vasomotor depression may occur with higher doses.

**CNS stimulants** include amphetamines and cocaine (including "crack"). These drugs have great abuse potential and may quickly produce psychological dependence. Cocaine, especially when smoked or inhaled, produces euphoria but may also change personality, cause seizures, and constrict certain blood vessels, leading to sudden death from stroke or cardiac arrhythmia. Cocaine's very rapid effect, and perhaps its addictiveness, reflect its rapid entry and metabolism in the brain. Cocaine arrives at the basal nuclei in four to six minutes and is mostly cleared within thirty minutes. The drug inhibits transporter molecules that remove dopamine from synapses after it is released. "Ecstasy" is a type of amphetamine.

**Hallucinogens** alter perceptions. They cause *illusions,* which are distortions of vision, hearing, taste, touch, and smell; *synesthesia,* such as "hearing" colors or "feeling" sounds; and hallucinations. The most commonly abused and most potent hallucinogen is lysergic acid diethylamide (LSD). LSD may act as an excitatory neurotransmitter. Persons under the influence of LSD may greatly overestimate their physical capabilities, such as believing they can fly off the top of a high building. Phencyclidine (PCP) is another abused hallucinogen. Its use can lead to prolonged psychosis that may provoke assault, murder, and suicide.

A traumatic brain injury (TBI) results from mechanical force. Mild TBI, also called a concussion, causes loss of consciousness or altered mental status. Disturbed sleep and problems with memory and balance may follow. A concussion is a temporary condition. However, repeated blows to the head, as can occur in playing football, can cause chronic traumatic encephalopathy. This more serious condition can lead to depression, headaches, and dementia. Severe TBI occurs in combat situations and is also called "blast-related brain injury." It may affect cognition (thinking) many years later.

### PRACTICE

49. Where is the cerebellum located?
50. What are the major functions of the cerebellum?

## 9.15 | Peripheral Nervous System

The peripheral nervous system (PNS) consists of nerves that branch from the CNS and connect it to other body parts. The PNS includes the cranial nerves, which arise

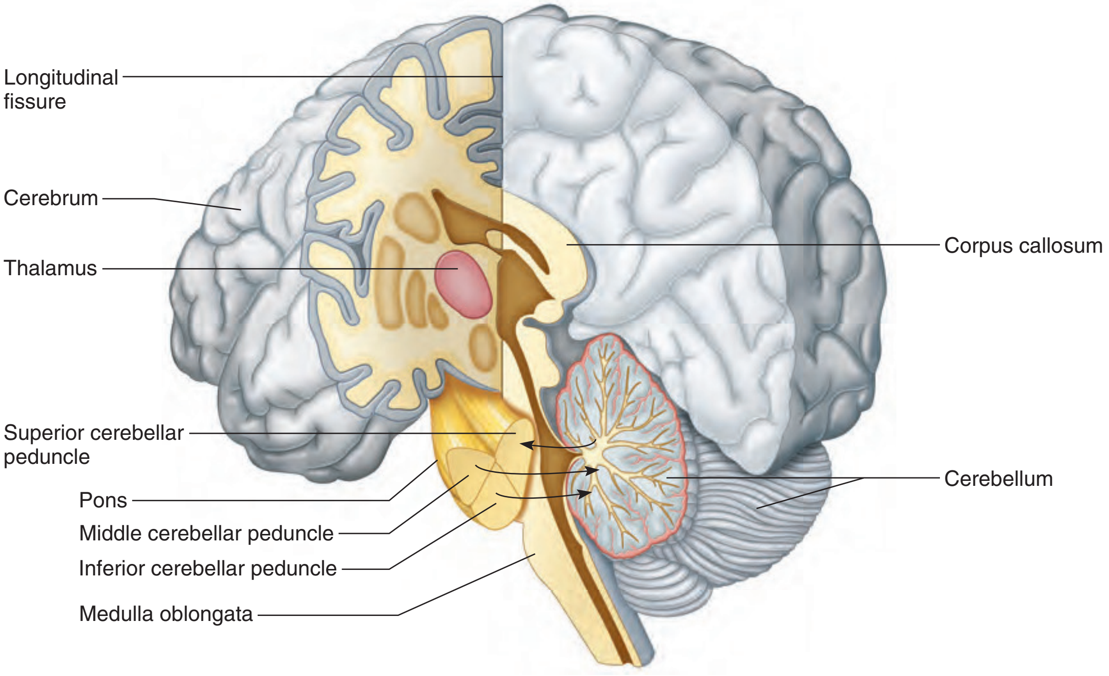

Longitudinal fissure
Cerebrum
Thalamus
Superior cerebellar peduncle
Pons
Middle cerebellar peduncle
Inferior cerebellar peduncle
Medulla oblongata
Corpus callosum
Cerebellum

**FIGURE 9.34** APR The cerebellum, which is located below the occipital lobes of the cerebrum, communicates with other parts of the nervous system by means of the cerebellar peduncles.

from the brain, and the spinal nerves, which arise from the spinal cord.

The PNS can also be subdivided into the somatic and autonomic nervous systems. Generally, the **somatic** (so-mat′ik) **nervous system** consists of the cranial and spinal nerve fibers that connect the CNS to the skin and skeletal muscles; it oversees conscious activities. The **autonomic** (aw″to-nom′ik) **nervous system** includes fibers that connect the CNS to viscera, such as the heart, stomach, intestines, and glands; it controls unconscious activities. Table 9.5 outlines the subdivisions of the nervous system (see fig. 9.2).

## Cranial Nerves

Twelve pairs of **cranial nerves** arise from the underside of the brain (fig. 9.35). Except for the first pair, which begins in the cerebrum, these nerves originate from the brainstem. They pass from their sites of origin through foramina of the skull and lead to parts of the head, neck, and trunk.

Most of the cranial nerves are mixed nerves containing both sensory and motor nerve fibers, but some of those associated with special senses, such as smell and vision, contain only sensory fibers. Other cranial nerves that affect muscles and glands are composed primarily of motor fibers.

Sensory fibers present in the cranial nerves have neuron cell bodies that are outside the brain, usually in groups called *ganglia.* On the other hand, motor neuron cell bodies are typically in the gray matter of the brain.

Numbers or names designate the cranial nerves. The numbers indicate the order in which the nerves arise from the front to the back of the brain, and the names describe their primary functions or the general distribution of their fibers (fig. 9.35).

The first pair of cranial nerves, the **olfactory nerves (I),** are associated with the sense of smell and contain axons only of sensory neurons. These bipolar neurons, located in the lining of the upper nasal cavity, serve as *olfactory receptor cells.* Axons from these receptors pass upward through the cribriform plates of the ethmoid bone, carrying impulses to the olfactory neurons in the *olfactory bulbs,* which are extensions of the cerebral cortex just beneath the frontal lobes (see fig. 10.4, p. 279). Sensory impulses are conducted from the olfactory bulbs along *olfactory tracts* to cerebral centers, where they are interpreted. The result of this interpretation is the sensation of smell.

The second pair of cranial nerves, the **optic nerves (II),** lead from the eyes to the brain and are associated with vision. The sensory nerve cell bodies of these nerve fibers

**TABLE 9.5 Subdivisions of the Nervous System**

1. Central nervous system (CNS)
   a. Brain
   b. Spinal cord
2. Peripheral nervous system (PNS)
   a. Cranial nerves arising from the brain and brainstem
      (1) Somatic fibers connecting to skin and skeletal muscles
      (2) Autonomic fibers connecting to viscera
   b. Spinal nerves arising from the spinal cord
      (1) Somatic fibers connecting to skin and skeletal muscles
      (2) Autonomic fibers connecting to viscera

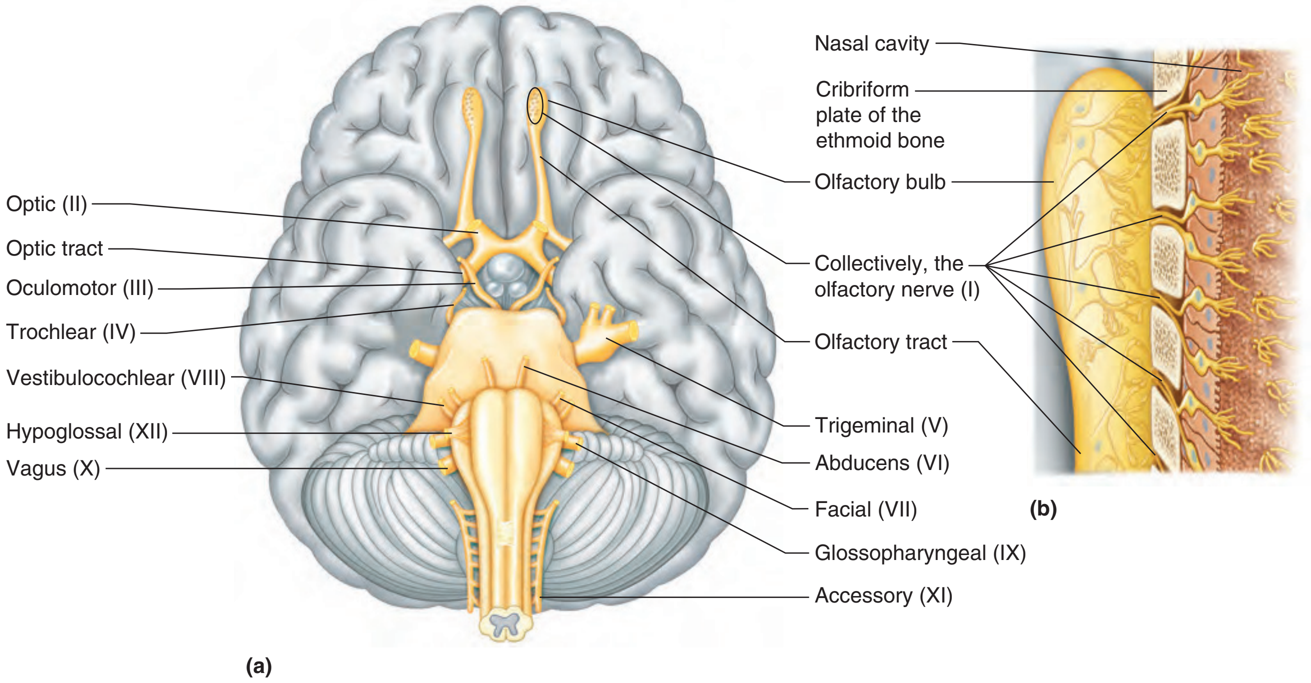


**FIGURE 9.35** APR The cranial nerves, except for the first pair, arise from the brainstem. **(a)** They are identified by numbers indicating their order, by their function, or by the general distribution of their fibers. **(b)** The collection of nerve fibers passing through the cribriform plate comprise the olfactory nerve (I).

are in ganglion cell layers in the eyes, and their axons pass through the *optic foramina* of the orbits and continue into the visual nerve pathways of the brain (see chapter 10, pp. 297–298). Sensory impulses conducted on the optic nerves are interpreted in the visual cortices of the occipital lobes.

The third pair of cranial nerves, the **oculomotor nerves (III),** arise from the midbrain and pass into the orbits of the eyes. One component of each nerve connects to the voluntary muscles that raise the eyelid and to four of the six muscles that move the eye. A second component of each oculomotor nerve is part of the autonomic nervous system and innervates involuntary muscles in the eyes. These muscles adjust the amount of light entering the eyes and focus the lenses.

The fourth pair of cranial nerves, the **trochlear nerves (IV),** arise from the midbrain and are the smallest cranial nerves. Each nerve conducts motor impulses to a fifth voluntary muscle that moves the eye and is not innervated by the oculomotor nerve.

The fifth pair of cranial nerves, the **trigeminal nerves (V),** are the largest cranial nerves and arise from the pons. They are mixed nerves, with the sensory parts more extensive than the motor parts. Each sensory component includes three large branches, called the ophthalmic, maxillary, and mandibular divisions.

The *ophthalmic division* of the trigeminal nerves consists of sensory fibers that conduct impulses to the brain from the surface of the eyes, the tear glands, and the skin of the anterior scalp, forehead, and upper eyelids. The fibers of the *maxillary division* conduct sensory impulses from the upper teeth, upper gum, and upper lip, as well as from the mucous lining of the palate and the skin of the face. The *mandibular division* includes both motor and sensory fibers. The sensory branches conduct impulses from the scalp behind the ears, the skin of the jaw, the lower teeth, the lower gum, and the lower lip. The motor branches innervate the muscles of mastication and certain muscles in the floor of the mouth.

The sixth pair of cranial nerves, the **abducens nerves (VI),** are quite small and originate from the pons near the medulla oblongata. Each nerve enters the orbit of the eye and innervates motor impulses to the remaining muscle that moves the eye.

The seventh pair of cranial nerves, the **facial nerves (VII),** arise from the lower part of the pons and emerge on the sides of the face. Their sensory branches are associated with taste receptors on the anterior two-thirds of the tongue, and some of their motor fibers conduct impulses to the muscles of facial expression. Still other motor fibers of these nerves function in the autonomic nervous system and stimulate secretions from tear glands and salivary glands.

The eighth pair of cranial nerves, the **vestibulocochlear nerves (VIII),** are sensory nerves that arise from the medulla oblongata. Each of these nerves has two distinct parts—a vestibular branch and a cochlear branch.

The neuron cell bodies of the *vestibular branch* fibers are located in ganglia associated with parts of the inner ear. These parts contain the receptors involved with reflexes that help maintain equilibrium. The neuron cell bodies of the *cochlear branch* fibers are located in the parts of the inner ear that house the hearing receptors. Information from these branches reaches the medulla oblongata and midbrain on its way to the temporal lobes, where it is interpreted.

The ninth pair of cranial nerves, the **glossopharyngeal nerves (IX),** are associated with the tongue and pharynx. These mixed nerves arise from the medulla oblongata, with predominantly sensory fibers. These sensory fibers conduct impulses from the linings of the pharynx, tonsils, and posterior third of the tongue to the brain. Fibers in the motor component innervate muscles of the pharynx that function in swallowing.

The tenth pair of cranial nerves, the **vagus nerves (X),** originate in the medulla oblongata and extend downward through the neck into the chest and abdomen. These nerves are mixed, containing both somatic and autonomic branches, with autonomic fibers predominant. Certain somatic motor fibers conduct impulses to muscles of the larynx that are associated with speech and swallowing. Autonomic motor fibers of the vagus nerves innervate the heart, smooth muscle, and glands in the thorax and abdomen.

The eleventh pair of cranial nerves, the **accessory nerves (XI),** originate in the medulla oblongata and the spinal cord; thus, they have both cranial and spinal branches. Each *cranial branch* joins a vagus nerve and conducts impulses to muscles of the soft palate, pharynx, and larynx. The *spinal branch* descends into the neck and innervates motor fibers to the trapezius and sternocleidomastoid muscles.

The twelfth pair of cranial nerves, the **hypoglossal nerves (XII),** arise from the medulla oblongata and pass into the tongue. They include motor fibers that conduct impulses to muscles that move the tongue in speaking, chewing, and swallowing. Table 9.6 summarizes the functions of the cranial nerves.

## PRACTICE

51. Define *peripheral nervous system.*
52. Distinguish between somatic and autonomic nerve fibers.
53. Name the cranial nerves, and list the major functions of each.

### TABLE 9.6 Functions of Cranial Nerves

| Nerve | Type | Function |
|---|---|---|
| I Olfactory | Sensory | Sensory fibers conduct impulses associated with the sense of smell. |
| II Optic | Sensory | Sensory fibers conduct impulses associated with the sense of vision. |
| III Oculomotor | Primarily motor | Motor fibers conduct impulses to muscles that raise eyelids, move eyes, adjust the amount of light entering the eyes, and focus lenses.<br>Some sensory fibers conduct impulses associated with the condition of muscles. |
| IV Trochlear | Primarily motor | Motor fibers conduct impulses to muscles that move the eyes.<br>Some sensory fibers conduct impulses associated with the condition of muscles. |
| V Trigeminal | Mixed | |
| Ophthalmic division | | Sensory fibers conduct impulses from the surface of the eyes, tear glands, scalp, forehead, and upper eyelids. |
| Maxillary division | | Sensory fibers conduct impulses from the upper teeth, upper gum, upper lip, lining of the palate, and skin of the face. |
| Mandibular division | | Sensory fibers conduct impulses from the skin of the jaw, lower teeth, lower gum, and lower lip.<br>Motor fibers conduct impulses to muscles of mastication and to muscles in the floor of the mouth. |
| VI Abducens | Primarily motor | Motor fibers conduct impulses to muscles that move the eyes.<br>Some sensory fibers conduct impulses associated with the condition of muscles. |
| VII Facial | Mixed | Sensory fibers conduct impulses associated with taste receptors of the anterior tongue. Motor fibers conduct impulses to muscles of facial expression, tear glands, and salivary glands. |
| VIII Vestibulocochlear | Sensory | |
| Vestibular branch | | Sensory fibers conduct impulses associated with the sense of equilibrium. |
| Cochlear branch | | Sensory fibers conduct impulses associated with the sense of hearing. |
| IX Glossopharyngeal | Mixed | Sensory fibers conduct impulses from the pharynx, tonsils, posterior tongue, and carotid arteries.<br>Motor fibers conduct impulses to muscles of the pharynx used in swallowing and to salivary glands. |
| X Vagus | Mixed | Somatic motor fibers conduct impulses to muscles associated with speech and swallowing; autonomic motor fibers conduct impulses to the heart, smooth muscle, and glands in the thorax and abdomen.<br>Sensory fibers conduct impulses from the pharynx, larynx, esophagus, and viscera of the thorax and abdomen. |
| XI Accessory | Primarily motor | |
| Cranial branch | | Motor fibers conduct impulses to muscles of the soft palate, pharynx, and larynx. |
| Spinal branch | | Motor fibers conduct impulses to muscles of the neck and back. |
| XII Hypoglossal | Primarily motor | Motor fibers conduct impulses to muscles that move the tongue. |

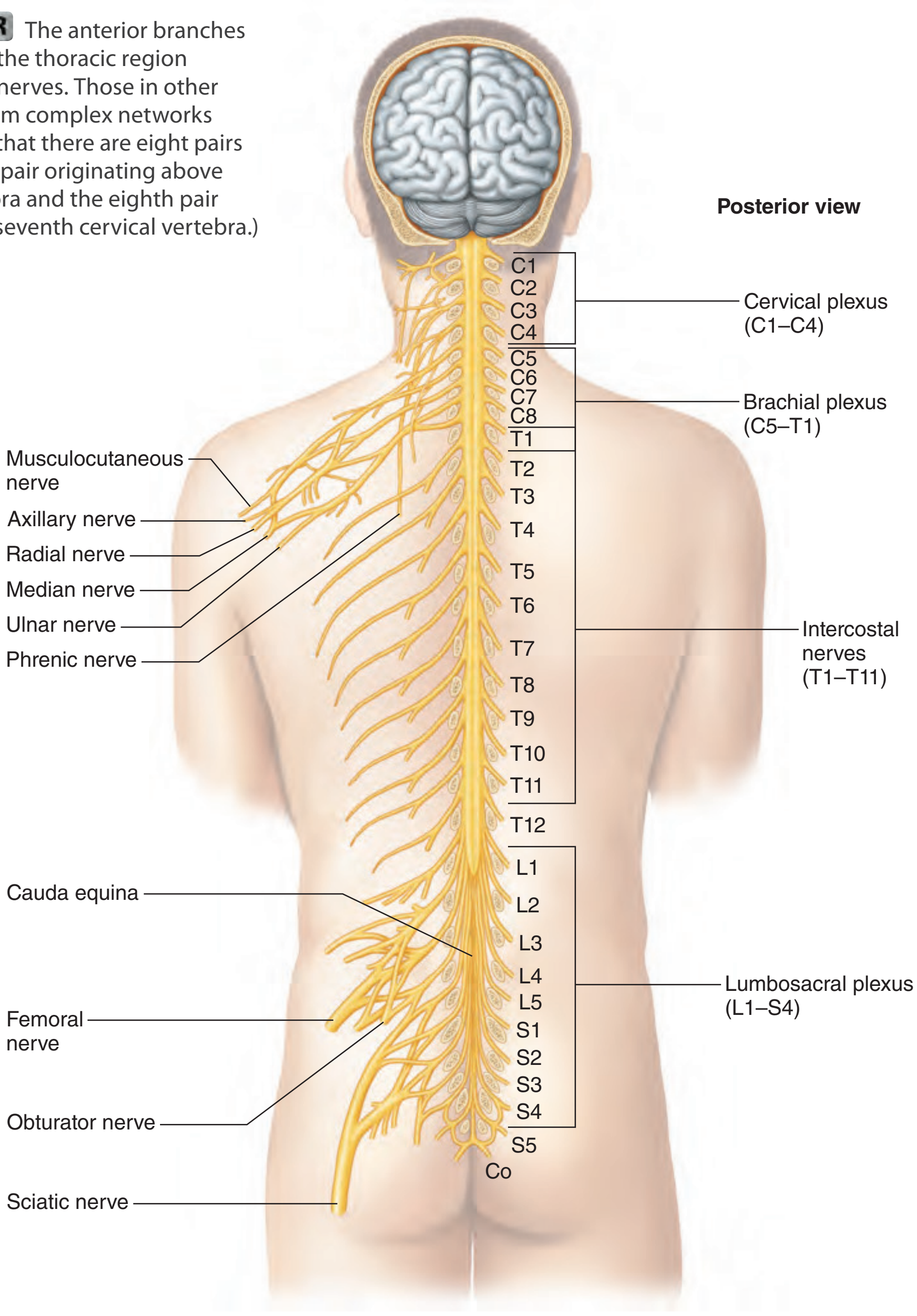
The consequences of a cranial nerve injury depend on the injury's location and extent. Damage to one member of a nerve pair will not cause a total loss of function, but injury to both nerves may. If a nerve is severed completely, functional loss of that nerve is total; if the cut is incomplete, loss may be partial.

## Spinal Nerves

Thirty-one pairs of **spinal nerves** originate from the spinal cord (fig. 9.36). All but the first pair are mixed nerves that provide two-way communication between the spinal cord and parts of the upper and lower limbs, neck, and trunk.

Spinal nerves are not named individually, but are grouped according to the level from which they arise. Each nerve is numbered in sequence. On each vertebra the vertebral notches, the major parts of the intervertebral foramina, are associated with the inferior part of their respective vertebrae. For this reason, each spinal nerve, as it passes through the intervertebral foramen, is associated with the vertebra above it. The cervical spinal nerves are an exception, because spinal nerve C1 passes superior to the vertebra C1. Thus, although there are seven cervical vertebrae, there are eight pairs of *cervical nerves* (numbered C1 to C8). There are twelve pairs of *thoracic nerves* (numbered T1 to T12), five pairs of *lumbar nerves* (numbered L1 to L5), five pairs of *sacral nerves* (numbered S1 to S5), and one pair of *coccygeal nerves* (Co).

**FIGURE 9.36** APR The anterior branches of the spinal nerves in the thoracic region give rise to intercostal nerves. Those in other regions combine to form complex networks called plexuses. (Note that there are eight pairs of cervical nerves, one pair originating above the first cervical vertebra and the eighth pair originating below the seventh cervical vertebra.)


Posterior view
C1
C2
C3
C4
C5
C6
C7
C8
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
T11
T12
L1
L2
L3
L4
L5
S1
S2
S3
S4
S5
Co
Cervical plexus (C1–C4)
Brachial plexus (C5–T1)
Intercostal nerves (T1–T11)
Lumbosacral plexus (L1–S4)
Musculocutaneous nerve
Axillary nerve
Radial nerve
Median nerve
Ulnar nerve
Phrenic nerve
Cauda equina
Femoral nerve
Obturator nerve
Sciatic nerve

The adult spinal cord ends at the level between the first and second lumbar vertebrae. The lumbar, sacral, and coccygeal nerves descend beyond the end of the cord, forming a structure called the *cauda equina* (horse's tail).

Each spinal nerve emerges from the cord by two short branches, or *roots,* which lie within the vertebral column. The **dorsal root** (posterior or sensory root) can be identified by an enlargement called the *dorsal root ganglion* (see fig. 9.23*a*). This ganglion contains the cell bodies of the unipolar sensory neurons whose axons (peripheral processes) conduct impulses inward from the peripheral body parts. The axons of these neurons (central processes) extend through the dorsal root and into the spinal cord, where they form synapses with dendrites of other neurons (see fig. 9.6). The **ventral root** (anterior or motor root) of each spinal nerve consists of axons from the motor neurons whose cell bodies are within the gray matter of the cord.

A ventral root and a dorsal root unite to form a spinal nerve, which extends outward from the vertebral canal through an *intervertebral foramen* (see fig. 7.17, p. 162). Just beyond its foramen, each spinal nerve divides into several parts.

Except in the thoracic region, the main parts of the spinal nerves combine to form complex networks called **plexuses** instead of continuing directly to peripheral body parts (fig. 9.36). In a plexus, spinal nerve axons are sorted and recombined so that axons that innervate a particular body part reach it in the same peripheral nerve, even though the axons originate from different spinal nerves.

### *Cervical Plexuses*

The **cervical plexuses** lie deep in the neck on either side and form from the branches of the first four cervical nerves. Axons from these plexuses supply the muscles and skin of the neck. In addition, axons from the third, fourth, and fifth cervical nerves pass into the right and left **phrenic nerves,** which conduct motor impulses to the muscle fibers of the diaphragm.

### *Brachial Plexuses*

Branches of the lower four cervical nerves and the first thoracic nerve give rise to the **brachial plexuses.** These networks of axons are deep within the shoulders between the neck and axillae (armpits). The major branches emerging from the brachial plexuses supply the muscles and skin of the arm, forearm, and hand, and include the **musculocutaneous, ulnar, median, radial,** and **axillary nerves.**

### *Lumbosacral Plexuses*

The **lumbosacral plexuses** are formed on either side by the last thoracic nerve and the lumbar, sacral, and coccygeal nerves. These networks of axons extend from the lumbar region of the back into the pelvic cavity, giving rise to a number of motor and sensory axons associated with the muscles and skin of the lower abdominal wall, external genitalia, buttocks, thighs, legs, and feet. The major branches of these plexuses include the **obturator, femoral,** and **sciatic nerves.**

The anterior branches of the thoracic spinal nerves do not enter a plexus. Instead, they enter spaces between the ribs and become **intercostal nerves.** These nerves supply motor impulses to the intercostal muscles and the upper abdominal wall muscles. They also receive sensory impulses from the skin of the thorax and abdomen.

**PRACTICE**

54. How are spinal nerves grouped?
55. Describe how a spinal nerve joins the spinal cord.
56. Name and locate the major nerve plexuses.

Spinal nerves may be injured in a variety of ways, including stabs, gunshot wounds, birth injuries, dislocations and fractures of the vertebrae, and pressure from tumors in surrounding tissues. For example, a sudden extension followed by flexion of the neck, called *whiplash,* can occur during rear-end automobile collisions and may stretch the superficial nerves of the cervical plexuses. Whiplash may cause continuing headaches and pain in the neck and skin, which the cervical nerves supply.

## 9.16 | Autonomic Nervous System

The **autonomic nervous system** is the part of the PNS that functions independently (autonomously) and continuously without conscious effort. This system controls visceral functions by regulating the actions of smooth muscle, cardiac muscle, and glands. It regulates heart rate, blood pressure, breathing rate, body temperature, and other activities that maintain homeostasis. Parts of the autonomic nervous system respond to emotional stress and prepare the body to meet the demands of strenuous physical activity.

### General Characteristics

Reflexes in which sensory signals originate from receptors in the viscera and the skin regulate autonomic activities. Axons conduct these signals to centers in the brain or spinal cord. In response, motor impulses travel out from these centers on axons in cranial and spinal nerves. These axons typically lead to ganglia. The impulses they conduct are integrated in these ganglia and relayed to effectors (muscles and glands) that respond by contracting, releasing secretions, or being inhibited. The integrative function of the ganglia provides the autonomic system with a degree of independence from the brain and spinal cord.

The autonomic nervous system includes two divisions—the **sympathetic** (sim″pah-thet′ik) and **parasympathetic** (par″ah-sim″pah-thet′ik) **divisions.** Some effectors are innervated by axons from each division. In such cases, impulses on one set of axons may activate an organ, while impulses on the other set inhibit it. Thus, the divisions may act antagonistically, alternately activating or inhibiting the actions of effectors.

The functions of the autonomic divisions are mixed; that is, each activates some organs and inhibits others. However, the divisions have important functional differences. The sympathetic division prepares the body for energy-expending, stressful, or emergency situations, as part of the *fight-or-flight* response. Conversely, the parasympathetic division is most active under ordinary, restful conditions. It also counterbalances the effects of the sympathetic division and restores the body to a resting state following a stressful experience. For example, during an emergency the sympathetic division increases heart rate; following the emergency, the parasympathetic division decreases heart rate.

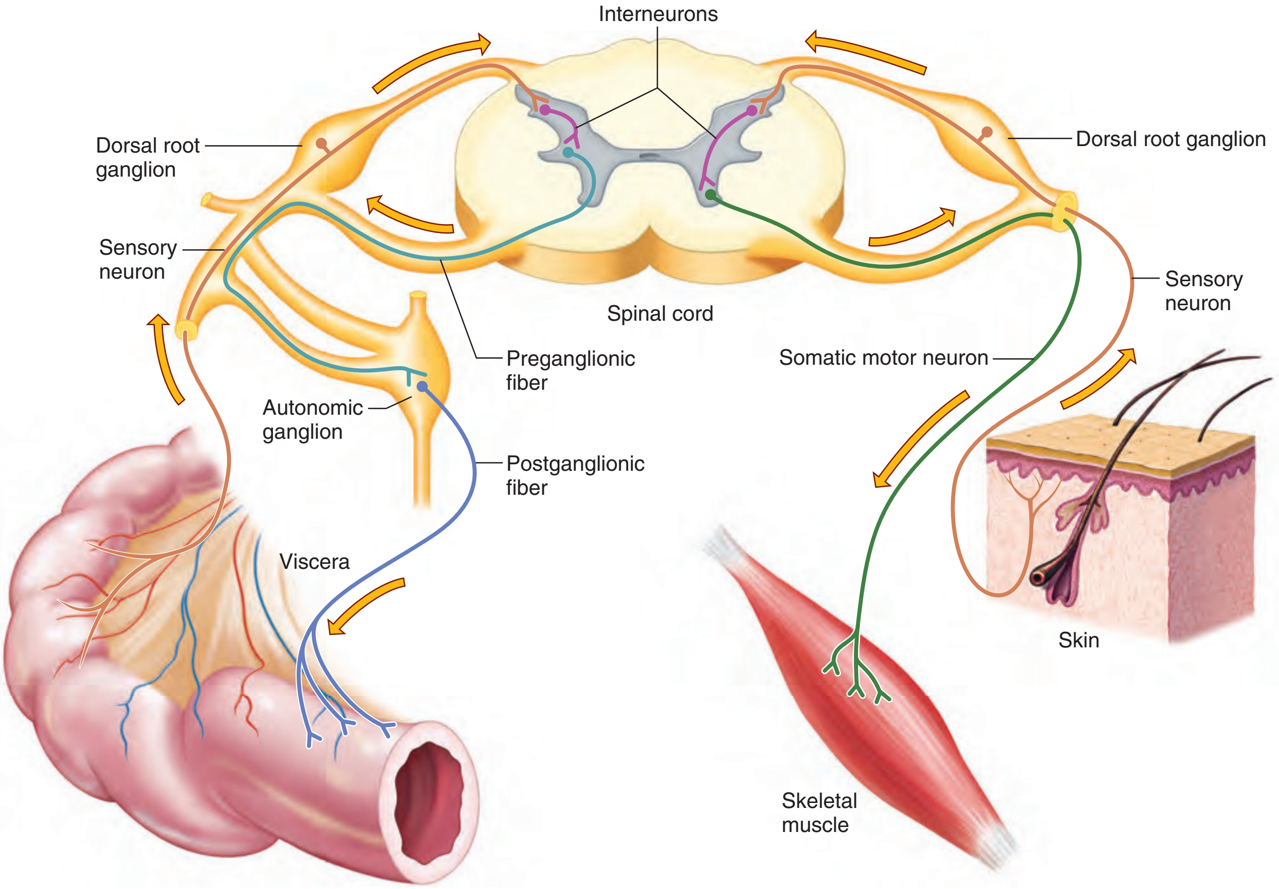
## Autonomic Neurons

The neurons of the autonomic nervous system are motor neurons. However, unlike the motor pathways of the somatic nervous system, which usually include a single neuron between the brain or spinal cord and a skeletal muscle, those of the autonomic system include two neurons (fig. 9.37). The cell body of the first, or preganglionic, neuron is located in the brain or spinal cord. Its axon, the **preganglionic fiber** (pre″gang-gle-on′ik fi′ber), leaves the CNS and synapses with one or more neurons whose cell bodies are located in the PNS within an autonomic ganglion. The axon of such a second neuron, or postganglionic neuron, is called a **postganglionic fiber** (pō st″gang-gle-on′ik fi′ber), and it extends to a visceral effector.

### *Sympathetic Division*

In the sympathetic division, the preganglionic fibers originate from neurons in the gray matter of the spinal cord (fig. 9.38). Their axons leave the cord through the ventral roots of spinal nerves in the first thoracic through the second lumbar segments. These fibers extend a short distance, then leave the spinal nerves, and each enters a member of a chain of sympathetic ganglia (*paravertebral ganglia*). One of these sympathetic chains extends longitudinally along each side of the vertebral column.

In paravertebral ganglia, preganglionic fibers form synapses with second neurons. The axons of these neurons, the postganglionic fibers, typically return to spinal nerves and extend to visceral effectors.



**(a)** Autonomic pathway

**(b)** Somatic pathway

**FIGURE 9.37** Motor pathways. **(a)** Autonomic pathways include two neurons between the CNS and an effector. **(b)** Somatic pathways usually have a single neuron between the CNS and an effector. Note that in both cases the motor fibers pass through the ventral root of the spinal cord.

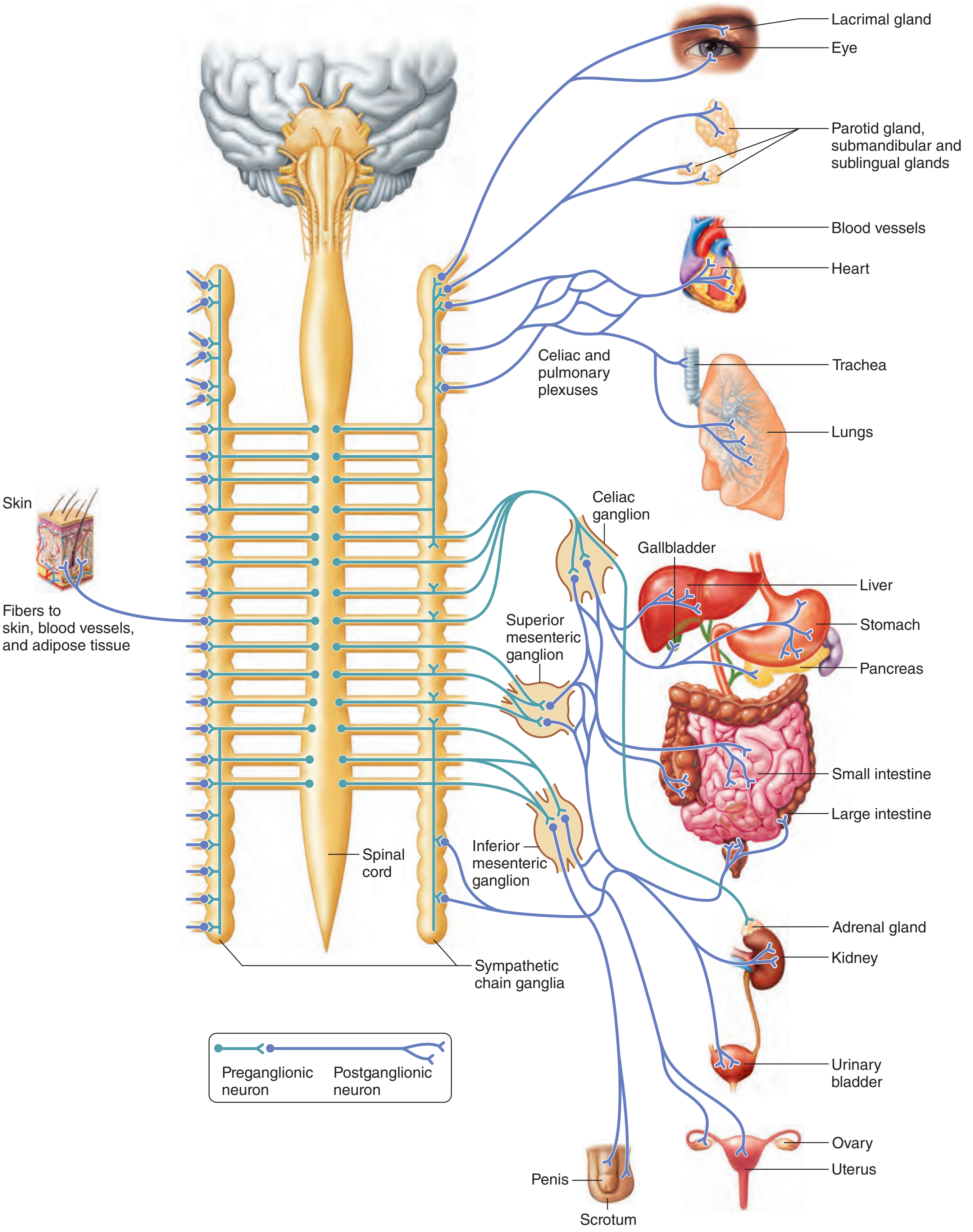

Lacrimal gland
Eye
Parotid gland, submandibular and sublingual glands
Blood vessels
Heart
Celiac and pulmonary plexuses
Trachea
Lungs
Skin
Fibers to skin, blood vessels, and adipose tissue
Celiac ganglion
Gallbladder
Liver
Stomach
Superior mesenteric ganglion
Pancreas
Small intestine
Large intestine
Spinal cord
Inferior mesenteric ganglion
Adrenal gland
Kidney
Sympathetic chain ganglia
Preganglionic neuron
Postganglionic neuron
Urinary bladder
Ovary
Uterus
Penis
Scrotum

**FIGURE 9.38** APR The preganglionic fibers of the sympathetic division of the autonomic nervous system arise from the thoracic and lumbar regions of the spinal cord (T1–L2). Note that the adrenal medulla is innervated directly by a preganglionic fiber.

### *Parasympathetic Division*

The preganglionic fibers of the parasympathetic division arise from the brainstem and sacral region of the spinal cord (fig. 9.39). From there, they lead outward in cranial or sacral nerves to ganglia located near or in various viscera. The relatively short postganglionic fibers continue from the ganglia to specific muscles or glands in these viscera.

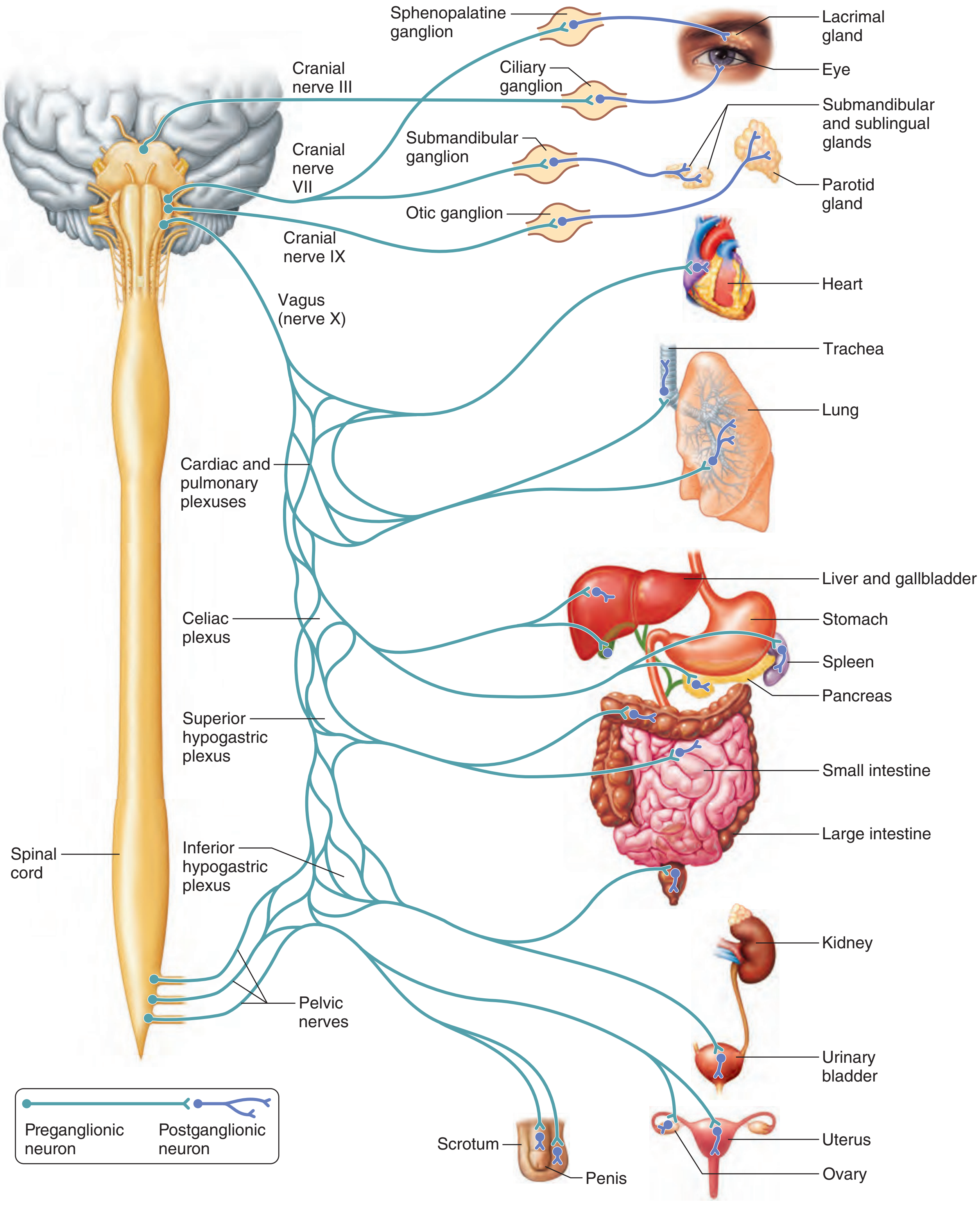

Sphenopalatine ganglion
Lacrimal gland
Cranial nerve III
Ciliary ganglion
Eye
Submandibular and sublingual glands
Cranial nerve VII
Submandibular ganglion
Parotid gland
Otic ganglion
Cranial nerve IX
Heart
Vagus (nerve X)
Trachea
Lung
Cardiac and pulmonary plexuses
Liver and gallbladder
Celiac plexus
Stomach
Spleen
Pancreas
Superior hypogastric plexus
Small intestine
Large intestine
Spinal cord
Inferior hypogastric plexus
Kidney
Pelvic nerves
Urinary bladder
Preganglionic neuron
Postganglionic neuron
Scrotum
Penis
Uterus
Ovary

**FIGURE 9.39** APR The preganglionic fibers of the parasympathetic division of the autonomic nervous system arise from the brainstem and sacral region of the spinal cord.

## PRACTICE

57. Describe the parts of the autonomic nervous system.
58. Distinguish between the divisions of the autonomic nervous system.
59. Describe a sympathetic nerve pathway and a parasympathetic nerve pathway.

## Autonomic Neurotransmitters

The preganglionic fibers of the sympathetic and parasympathetic divisions all secrete *acetylcholine* and are therefore called **cholinergic fibers** (ko″lin-er′jik fi′berz). The parasympathetic postganglionic fibers are also cholinergic. One exception, parasympathetic neurons that secrete nitric oxide, is described in chapter 19 (p. 525). However, most sympathetic postganglionic neurons secrete *norepinephrine* (noradrenalin) and are called **adrenergic fibers** (ad″ren-ur′jik fi′berz) (fig. 9.40). The different postganglionic neurotransmitters cause the different effects that the sympathetic and parasympathetic divisions have on their effector organs.

Most organs receive innervation from both sympathetic and parasympathetic divisions, usually with opposing actions. For example, parasympathetic activity increases activity of the digestive system, whereas sympathetic activity decreases it. Similarly, sympathetic stimulation increases heart rate, but parasympathetic action slows heart rate.

Some viscera are controlled primarily by one division or the other. That is, the divisions are not always actively antagonistic. For example, the sympathetic division regulates the diameter of most blood vessels, which lack parasympathetic innervation. Smooth muscle in the walls of these vessels is continuously stimulated and thus is in a state of partial contraction (sympathetic tone). Decreasing sympathetic stimulation relaxes the muscular walls of the vessels, which increases the diameter of the vessels (dilates). Conversely, increasing sympathetic stimulation constricts the vessels. Table 9.7 summarizes the effects of stimulation by adrenergic and cholinergic fibers on some visceral effectors.

## Control of Autonomic Activity

The brain and spinal cord largely control the autonomic nervous system, although it has some independence resulting from the integrative function of its ganglia. For example, control centers in the medulla oblongata for cardiac, vasomotor, and respiratory activities receive sensory impulses from viscera on vagus nerve fibers and use autonomic nerve pathways to stimulate motor responses in the heart, blood vessels, and lungs. Similarly, the hypothalamus helps regulate body temperature, hunger, thirst, and water and electrolyte balance by influencing autonomic pathways.

More complex centers in the brain, including the limbic system and the cerebral cortex, control the autonomic nervous system during emotional stress. These structures utilize autonomic pathways to regulate emotional expression and behavior.

## PRACTICE

60. Which neurotransmitters operate in the autonomic nervous system?
61. How do the divisions of the autonomic nervous system regulate visceral activities?
62. How are autonomic activities controlled?

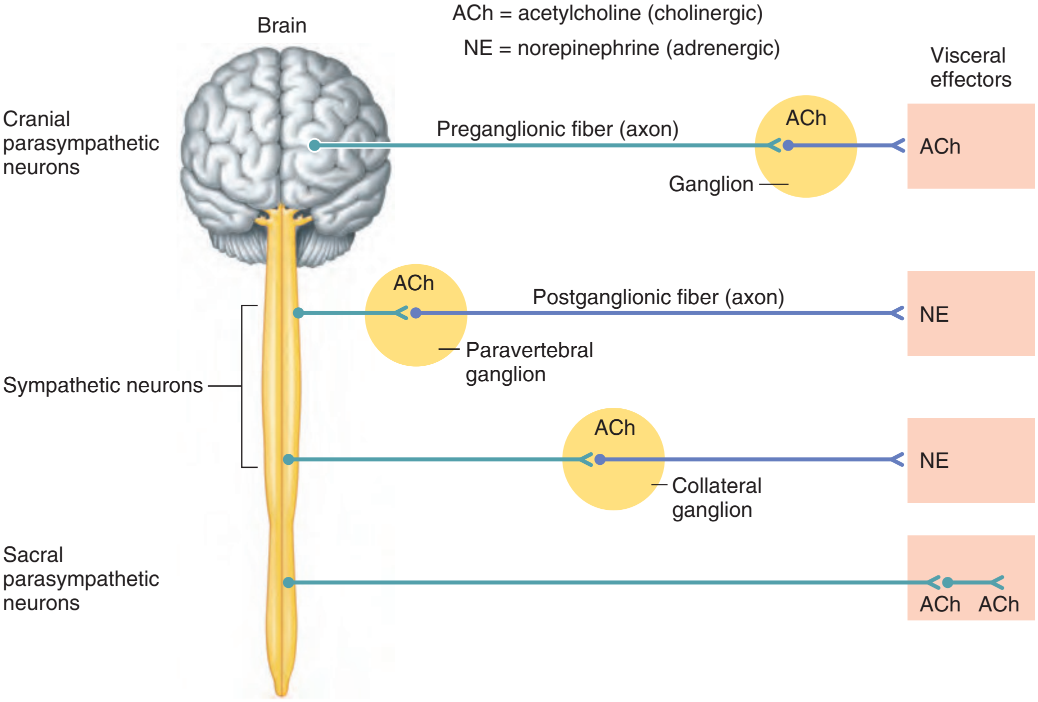
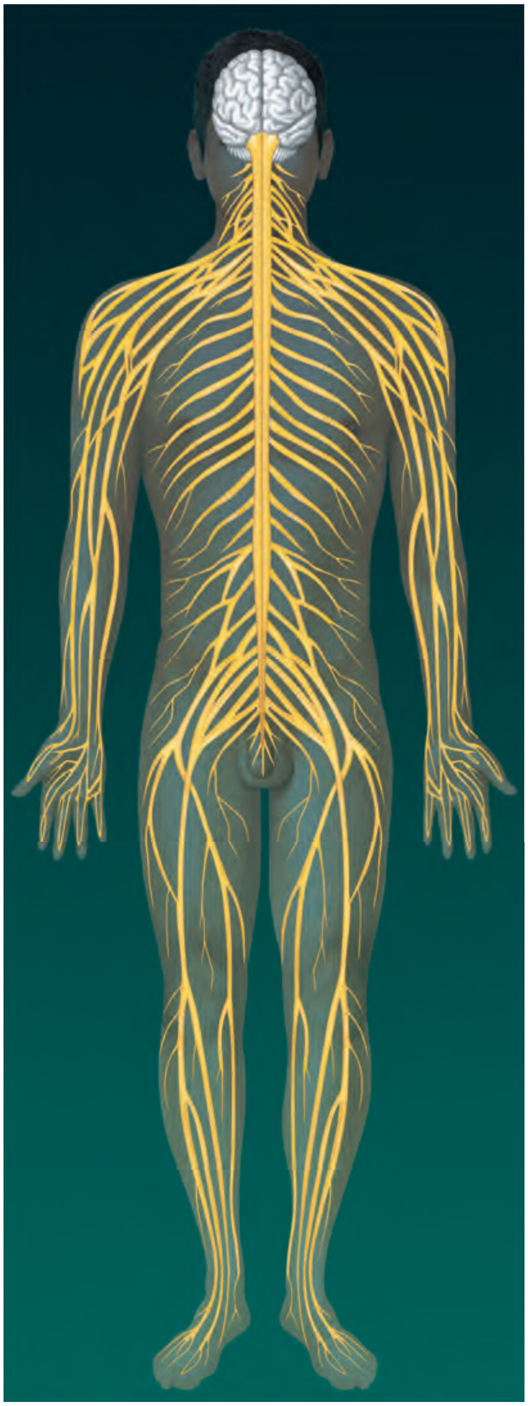

Brain
ACh = acetylcholine (cholinergic)
NE = norepinephrine (adrenergic)
Visceral effectors
Cranial parasympathetic neurons
Preganglionic fiber (axon)
ACh
ACh
Ganglion
ACh
Postganglionic fiber (axon)
NE
Paravertebral ganglion
Sympathetic neurons
ACh
NE
Collateral ganglion
Sacral parasympathetic neurons
ACh ACh

**FIGURE 9.40** Most sympathetic fibers are adrenergic and secrete norepinephrine at the ends of the postganglionic fiber; parasympathetic fibers are cholinergic and secrete acetylcholine at the ends of the postganglionic fibers. Two arrangements of parasympathetic postganglionic fibers are seen in both the cranial and sacral portions. Similarly, sympathetic paravertebral and collateral ganglia are seen in both the thoracic and lumbar portions of the nervous system. (Note: This representation does not show dendrites.)

# Nervous System



Neurons conduct impulses that allow body systems to communicate.

## Integumentary System

Sensory receptors provide the nervous system with information about the outside world.

## Skeletal System

Bones protect the brain and spinal cord and help maintain plasma calcium, which is important to neuron function.

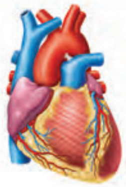
## Muscular System

The nervous system controls movement and processes information about the position of body parts.

## Endocrine System

The hypothalamus controls secretion of many hormones.

## Cardiovascular System



The nervous system helps control blood flow and blood pressure.

## Lymphatic System

Stress may impair the immune response.

## Digestive System

The nervous system can influence digestive function.

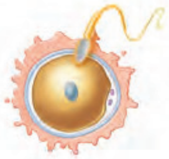
## Respiratory System

The nervous system alters respiratory activity to control oxygen levels and blood pH.

## Urinary System

The nervous system plays a role in urine production and elimination.

## Reproductive System



The nervous system plays a role in egg and sperm formation, sexual pleasure, childbirth, and nursing.

**TABLE 9.7 Effects of Neurotransmitter Substances on Visceral Effectors or Actions**

| Visceral Effector or Action | Response to Adrenergic Stimulation (Sympathetic) | Response to Cholinergic Stimulation (Parasympathetic) |
|---|---|---|
| Pupil of the eye | Dilation | Constriction |
| Heart rate | Increases | Decreases |
| Bronchioles of lungs | Dilation | Constriction |
| Muscles of intestinal wall | Slows peristaltic action | Speeds peristaltic action |
| Intestinal glands | Secretion decreases | Secretion increases |
| Blood distribution | More blood to skeletal muscles; less blood to digestive organs | More blood to digestive organs; less blood to skeletal muscles |
| Blood glucose concentration | Increases | Decreases |
| Salivary glands | Secretion decreases | Secretion increases |
| Tear glands | No action | Secretion |
| Muscles of gallbladder | Relaxation | Contraction |
| Muscles of urinary bladder | Relaxation | Contraction |

## Summary Outline

### 9.1 Introduction (p. 224)

1. Nervous tissue includes neurons, which are the structural and functional units of the nervous system, and neuroglia.
2. Organs of the nervous system are divided into the central and peripheral nervous systems.

### 9.2 General Functions of the Nervous System (p. 225)

1. Sensory functions involve receptors that detect internal and external changes.
2. Integrative functions collect sensory information and make decisions that motor functions carry out.
3. Motor functions stimulate effectors to respond.

### 9.3 Neuroglia (p. 226)

1. Neuroglia in the central nervous system include microglial cells, oligodendrocytes, astrocytes, and ependymal cells.
2. In the peripheral nervous system, Schwann cells form myelin sheaths.

### 9.4 Neurons (p. 228)

1. A neuron includes a cell body, dendrites, and an axon.
2. Dendrites and the cell body provide receptive surfaces.
3. A single axon arises from the cell body and may be enclosed in a myelin sheath and a neurilemma.
4. Classification of neurons
    a. Neurons are classified structurally as multipolar, bipolar, or unipolar.
    b. Neurons are classified functionally as sensory neurons, interneurons, or motor neurons.

### 9.5 The Synapse (p. 232)

*A synapse is a junction between two neurons.*

1. A presynaptic neuron conducts an impulse into a synapse; a postsynaptic neuron responds.
2. Axons have synaptic knobs at their distal ends, which secrete neurotransmitters.
3. A neurotransmitter is released when an impulse reaches the end of an axon.
4. A neurotransmitter reaching the postsynaptic neuron membrane is either excitatory or inhibitory.

### 9.6 Cell Membrane Potential (p. 232)

*A cell membrane is usually polarized as a result of unequal ion distribution.*

1. Distribution of ions
    a. Pores and channels in cell membranes that allow passage of some ions but not others set up differences in the concentrations of specific ions inside and outside a neuron.
    b. Potassium ions pass more easily through cell membranes than do sodium ions.
2. Resting potential
    a. A high concentration of sodium ions is outside a cell membrane, and a high concentration of potassium ions is inside.
    b. Many negatively charged ions are inside a cell.
    c. In a resting cell, more positive ions leave than enter, so the outside of the cell membrane develops a positive charge, while the inside develops a negative charge.
3. Potential changes
    a. Stimulation of a cell membrane affects the membrane's resting potential.
    b. When its resting potential becomes less negative, a membrane becomes depolarized.
    c. Potential changes are graded.
    d. Achieving threshold potential triggers an action potential.
4. Action potential
    a. At threshold, sodium channels open, and sodium ions diffuse inward, depolarizing the membrane.
    b. At almost the same time, potassium channels open, and potassium ions diffuse outward, repolarizing the membrane.
    c. This rapid sequence of depolarization and repolarization is an action potential.
    d. Many action potentials can occur in a neuron without disrupting the ion concentrations. Active transport contributes to maintaining these concentrations.

### 9.7 Impulse Conduction (p. 236)

*A wave of action potentials is an impulse.*

1. Impulse conduction (action potential propagation)
    a. Unmyelinated axons conduct action potentials along their entire lengths.
    b. Myelinated axons conduct impulses more rapidly.

   c. Axons with larger diameters conduct impulses faster than those with smaller diameters.
2. All-or-none response
   a. An action potential occurs in an all-or-none manner whenever a stimulus of threshold intensity is applied to an axon.
   b. All of the action potentials triggered on an axon are of the same strength.

### 9.8 Synaptic Transmission (p. 239)

1. Excitatory and inhibitory actions
   a. Neurotransmitters that trigger impulses are excitatory. Those that inhibit impulses are inhibitory.
   b. The net effect of synaptic knobs communicating with a neuron depends on which knobs are activated from moment to moment.
2. Neurotransmitters
   a. The nervous system produces many different neurotransmitters.
   b. Neurotransmitters include acetylcholine, biogenic amines, amino acids, and peptides.
   c. A synaptic knob releases neurotransmitters when an action potential increases membrane permeability to calcium ions.
   d. After being released, neurotransmitters are decomposed or removed from synaptic clefts.

### 9.9 Impulse Processing (p. 240)

*How the nervous system processes and responds to impulses reflects the organization of neurons in the brain and spinal cord.*

1. Neuronal pools
   a. Neurons form pools in the central nervous system.
   b. Each pool receives impulses, processes them, and conducts impulses away.
2. Facilitation
   a. Each neuron in a pool may receive excitatory and inhibitory stimuli.
   b. A neuron is facilitated when it receives subthreshold stimuli and becomes more excitable.
3. Convergence
   a. Impulses from two or more incoming axons may converge on a single neuron.
   b. Convergence enables impulses from different sources to have an additive effect on a neuron.
4. Divergence
   a. Impulses leaving a pool may diverge by passing into several output neurons.
   b. Divergence amplifies impulses.

### 9.10 Types of Nerves (p. 241)

1. Nerves are cordlike bundles (fascicles) of nerve fibers (axons).
2. Nerves are sensory, motor, or mixed, depending on which type of axons they contain.

### 9.11 Nerve Pathways (p. 242)

*A nerve pathway is the route an impulse follows through the nervous system.*

1. A reflex arc usually includes a sensory neuron, a reflex center composed of interneurons, and a motor neuron.
2. Reflex behavior
   a. Reflexes are automatic, subconscious responses to changes.
   b. They help maintain homeostasis.
   c. Two neurons carry out the patellar reflex. It is therefore monosynaptic.
   d. Withdrawal reflexes are protective.

### 9.12 Meninges (p. 243)

1. Bone and meninges surround the brain and spinal cord.
2. The meninges are the dura mater, arachnoid mater, and pia mater.
3. Cerebrospinal fluid fills the space between the arachnoid and pia maters.

### 9.13 Spinal Cord (p. 245)

*The spinal cord is a nerve column that extends from the brain into the vertebral canal.*

1. Structure of the spinal cord
   a. Each of the spinal cord's thirty-one segments gives rise to a pair of spinal nerves (two pairs are associated with C1).
   b. The spinal cord has a cervical enlargement and a lumbar enlargement.
   c. A central core of gray matter lies within white matter.
   d. White matter consists of bundles of myelinated axons called tracts.
2. Functions of the spinal cord
   a. The spinal cord provides a two-way communication system between the brain and other body parts and serves as a center for spinal reflexes.
   b. Ascending tracts conduct sensory impulses to the brain. Descending tracts conduct motor impulses to muscles and glands.

### 9.14 Brain (p. 247)

*The brain is subdivided into the cerebrum, diencephalon, brainstem, and cerebellum.*

1. Structure of the cerebrum
   a. The cerebrum consists of two cerebral hemispheres connected by the corpus callosum.
   b. The cerebral cortex is a thin layer of gray matter near the surface.
   c. White matter consists of myelinated axons that connect neurons in the nervous system and communicate with other body parts.
2. Functions of the cerebrum
   a. The cerebrum provides higher brain functions.
   b. The cerebral cortex consists of sensory, association, and motor, areas.
   c. One cerebral hemisphere usually dominates for certain intellectual functions.
3. Ventricles and cerebrospinal fluid
   a. Ventricles are interconnected cavities within the cerebral hemispheres and brainstem.
   b. Cerebrospinal fluid fills the ventricles.
   c. The choroid plexuses in the walls of the ventricles secrete cerebrospinal fluid.
4. Diencephalon
   a. The diencephalon contains the thalamus, which is a central relay station for incoming sensory impulses, and the hypothalamus, which maintains homeostasis.
   b. The limbic system produces emotions and modifies behavior.
5. Brainstem
   a. The brainstem consists of the midbrain, pons, and medulla oblongata.
   b. The midbrain contains reflex centers associated with eye and head movements.
   c. The pons relays impulses between the cerebrum and other parts of the nervous system and contains centers that may help regulate breathing.
   d. The medulla oblongata relays all ascending and descending impulses and contains several vital and nonvital reflex centers.
   e. The reticular formation filters incoming sensory impulses, arousing the cerebral cortex into wakefulness when significant impulses arrive.

6. Cerebellum
    a. The cerebellum consists of two hemispheres.
    b. It functions primarily as a reflex center for integrating sensory information required in the coordination of skeletal muscle movements and the maintenance of equilibrium.

**9.15 Peripheral Nervous System (p. 257)**

*The peripheral nervous system consists of cranial and spinal nerves that branch from the brain and spinal cord to all body parts. It is also subdivided into the somatic and autonomic systems.*

1. Cranial nerves
    a. Twelve pairs of cranial nerves connect the brain to parts in the head, neck, and trunk.
    b. Most cranial nerves are mixed, but some are purely sensory, and others are primarily motor.
    c. The names of the cranial nerves indicate their primary functions or the general distributions of their fibers.
2. Spinal nerves
    a. Thirty-one pairs of spinal nerves originate from the spinal cord.
    b. These mixed nerves provide a two-way communication system between the spinal cord and parts of the upper and lower limbs, neck, and trunk.
    c. Spinal nerves are grouped according to the levels from which they arise, and they are numbered in sequence.
    d. Each spinal nerve emerges by a dorsal and a ventral root.
    e. Each spinal nerve divides into several branches just beyond its foramen.
    f. Most spinal nerves combine to form plexuses in which nerve fibers are sorted and recombined so that those fibers associated with a particular part reach it together.

**9.16 Autonomic Nervous System (p. 262)**

*The autonomic nervous system functions without conscious effort. It regulates the visceral activities that maintain homeostasis.*

1. General characteristics
    a. Autonomic functions are reflexes controlled from nerve centers in the brain and spinal cord.
    b. The autonomic nervous system consists of two divisions—the sympathetic and the parasympathetic.
    c. The sympathetic division responds to stressful and emergency conditions.
    d. The parasympathetic division is most active under ordinary conditions.
2. Autonomic nerve fibers
    a. Autonomic nerve fibers are motor fibers.
    b. Sympathetic fibers leave the spinal cord and synapse in paravertebral ganglia.
    c. Parasympathetic fibers begin in the brainstem and sacral region of the spinal cord and synapse in ganglia near viscera.
3. Autonomic neurotransmitters
    a. Sympathetic and parasympathetic preganglionic fibers secrete acetylcholine.
    b. Parasympathetic postganglionic fibers secrete acetylcholine. Sympathetic postganglionic fibers secrete norepinephrine.
    c. The different effects of the autonomic divisions are due to the different neurotransmitters the postganglionic fibers release.
    d. The two divisions usually have opposite actions.
4. Control of autonomic activity
    a. The autonomic nervous system is somewhat independent.
    b. Control centers in the medulla oblongata and hypothalamus utilize autonomic nerve pathways.
    c. The limbic system and cerebral cortex control the autonomic system during emotional stress.

## CHAPTER ASSESSMENTS

### 9.1 Introduction

**1.** The general function of neurons is to __________ , whereas the general functions of neuroglia are to __________ . (p. 224)

**2.** Match the neuron part on the left to its description on the right. (p. 224)

(1) dendrite
(2) axon
(3) cell body

A. a cell process that sends information
B. one of usually several cell processes that receive information
C. the rounded part of a neuron

**3.** Explain the relationship between the CNS and the PNS. (p. 225)

### 9.2 General Functions of the Nervous System

**4.** List the general functions of the nervous system. (p. 225)

### 9.3 Neuroglia

**5.** Match the types of neuroglia to their functions. (p. 226)

(1) ependymal cells
(2) oligodendrocytes
(3) astrocytes
(4) Schwann cells
(5) microglial cells

A. form a myelin sheath around peripheral nerves
B. phagocytize cellular debris and bacteria
C. line inner parts of ventricles and spinal cord
D. form scar tissue and regulate ion and nutrient concentrations in the CNS
E. form a myelin sheath around neurons in the CNS

### 9.4 Neurons

**6.** Describe three structures found in neurons that are also in other cell types, and describe two structures that are unique to neurons. (p. 228)

**7.** The part of a Schwann cell that contributes to the myelin sheath is the __________ , and the part that contributes to the neurilemma is the __________ . (p. 228)

**8.** Distinguish between myelinated and unmyelinated axons. (p. 228)

**9.** Distinguish among multipolar, bipolar, and unipolar neurons. (pp. 228–231)

**10.** Distinguish among sensory neurons, interneurons, and motor neurons. (p. 231)

**11.** Distinguish between ganglia and nuclei. (p. 231)

### 9.5 The Synapse

**12.** Define *synapse.* (p. 232)

**13.** Explain how information passes from one neuron to another. (p. 232)

### 9.6 Cell Membrane Potential

**14.** Explain how a membrane becomes polarized. (p. 232)

**15.** Describe how ions associated with nerve cell membranes are distributed. (p. 233)

**16.** Define *resting potential.* (p. 234)

**17.** Explain the relationship between threshold potential and an action potential. (p. 236)

**18.** List the events that occur during an action potential. (p. 236)

### 9.7 Impulse Conduction

**19.** Choose the correct sequence of events along an axon: (p. 236)

a. Resting potentials are propagated along a stimulated axon, causing a very small action potential.

b. A threshold stimulus opens $K^+$ channels and the ions diffuse in, depolarizing the cell membrane. Then $Na^+$ channels open, $Na^+$ exits, and the cell membrane repolarizes, generating an action potential that stimulates adjacent cell membrane, forming the impulse.

c. A threshold stimulus opens $Na^+$ channels and the ions diffuse in, depolarizing the cell membrane. Then $K^+$ channels open, $K^+$ exits, and the cell membrane repolarizes, generating an action potential that stimulates adjacent cell membrane, forming the impulse.

d. A threshold stimulus opens $Na^+$ channels and the ions diffuse in, depolarizing the cell membrane. Then $K^+$ channels open, $K^+$ exits, and the cell membrane repolarizes, generating an action potential that inhibits adjacent cell membrane, forming the impulse.

**20.** Explain why a myelin sheath covering an entire axon (with no nodes of Ranvier) would inhibit conduction of an impulse. (p. 236)

**21.** "All-or-none" response in impulse conduction means that ____________ . (p. 238)

### 9.8 Synaptic Transmission

**22.** Distinguish between excitatory and inhibitory actions of neurotransmitters. (p. 239)

**23.** Neurotransmitters are synthesized in ____________ and are stored in ____________ . (p. 239)

**24.** Match the neurotransmitter to its description on the right. (p. 239)

(1) biogenic amine
(2) acetylcholine
(3) neuropeptide
(4) GABA

A. short chains of amino acids
B. a modified amino acid
C. an amino acid
D. stimulates skeletal muscle contraction

**25.** Explain what happens to neurotransmitters after they are released. (pp. 239–240)

### 9.9 Impulse Processing

**26.** Describe the components of a neuronal pool. (p. 240)

**27.** "Facilitation in a neuronal pool" refers to ____________. (p. 241)

**28.** Distinguish between convergence and divergence in a neuronal pool. (p. 241)

### 9.10 Types of Nerves

**29.** Describe how sensory, motor, and mixed nerves differ. (p. 241)

### 9.11 Nerve Pathways

**30.** Distinguish between a reflex arc and a reflex. (p. 242)

**31.** Describe the components of a reflex arc and their functions. (p. 242)

**32.** List three body functions that reflexes control. (p. 242)

### 9.12 Meninges

**33.** Match each layer of the meninges to its description. (pp. 243–244)

(1) dura mater
(2) arachnoid mater
(3) pia mater

A. the thin, innermost layer, containing blood vessels and nerves
B. the tough, outermost layer, consisting mostly of connective tissue
C. the lacy membrane, lacking blood vessels, sandwiched between the other two layers

### 9.13 Spinal Cord

**34.** Describe the structure of the spinal cord. (p. 245)

**35.** Distinguish between the ascending and descending tracts of the spinal cord. (p. 246)

### 9.14 Brain

**36.** Name the four major parts of the brain and describe their general functions. (p. 247)

**37.** The area of the brain that contains centers controlling visceral activities is the ____________ . (p. 247)

a. cerebrum
b. cerebellum
c. brainstem
d. diencephalon

**38.** The structure that connects the cerebral hemispheres is the ____________ . (p. 247)

**39.** Distinguish between a sulcus and a fissure. (p. 247)

**40.** Relate the lobes of the cerebral hemispheres to the skull bones. (p. 248)

**41.** Locate the sensory, association, and motor areas of the cerebral cortex, and describe the general functions of each. (p. 250)

**42.** Define *hemisphere dominance.* (p. 251)

**43.** The function of the basal nuclei is to ____________ . (p. 252)

**44.** Locate the ventricles in the brain. (p. 252)

**45.** Explain how cerebrospinal fluid is produced and how it functions. (p. 252)

**46.** The part of the diencephalon that regulates hunger, weight, water and electrolyte balance, sleep and wakefulness, temperature, arterial blood pressure, heart rate, production of substances that stimulate the pituitary gland, and movement and secretion in areas of the digestive tract is the ____________ . (p. 254)

a. thalamus
b. pineal gland
c. infundibulum
d. hypothalamus

**47.** Define *limbic system,* and explain its functions. (p. 254)

**48.** The parts of the brainstem are the ____________ , ____________ , and ____________ . (p. 255)

**49.** List the functions of the three parts of the brainstem. (p. 255)

**50.** Vomiting is controlled by ____________ . (p. 255)

a. the reticular formation
b. the medulla oblongata
c. the midbrain
d. the pons

**51.** Describe what happens to the body when the reticular formation receives sensory impulses, and what happens when it does not receive stimulation. (p. 255)

**52.** Describe the functions of the cerebellum. (p. 256)

### 9.15 Peripheral Nervous System

**53.** Distinguish between cranial nerves and spinal nerves. (pp. 257–258)

**54.** Distinguish between the somatic nervous system and the autonomic nervous system. (p. 258)

**55.** Match the cranial nerves to the body parts or functions that they affect. More than one nerve pair may correspond to the same structure or function. (pp. 258–260)

(1) olfactory nerves (I)
(2) optic nerves (II)
(3) oculomotor nerves (III)
(4) trochlear nerves (IV)
(5) trigeminal nerves (V)
(6) abducens nerves (VI)
(7) facial nerves (VII)
(8) vestibulocochlear nerves (VIII)
(9) glossopharyngeal nerves (IX)
(10) vagus nerves (X)
(11) accessory nerves (XI)
(12) hypoglossal nerves (XII)

A. vision
B. hearing and equilibrium
C. muscles of the larynx, pharynx, soft palate, sternocleidomastoid and trapezius muscles
D. heart, various smooth muscles and glands in the thorax and abdomen
E. taste, facial expressions, secretion of tears and saliva
F. sense of smell
G. tongue movements and swallowing
H. face and scalp
I. eye movements

**56.** Explain how the spinal nerves are classified and numbered. (p. 261)

**57.** Describe the structure of a spinal nerve. (p. 262)

**58.** Define *plexus*, and locate the major plexuses of the spinal nerves. (p. 262)

### 9.16 Autonomic Nervous System

**59.** Describe the general functions of the autonomic nervous system. (p. 262)

**60.** Distinguish between the sympathetic and parasympathetic divisions of the autonomic nervous system. (p. 262)

**61.** Distinguish between preganglionic and postganglionic neurons. (p. 263)

**62.** The effects of the sympathetic and parasympathetic autonomic divisions differ because ____________ . (pp. 263–265)

**63.** List two ways in which the CNS controls autonomic activities. (p. 266)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 3.4, 9.3, 9.4

**1.** State two reasons why rapidly growing brain cancers are composed of neuroglia rather than neurons.

### OUTCOMES 9.3, 9.4, 9.7, 9.13, 9.14

**2.** In multiple sclerosis, nerve fibers in the CNS lose their myelin. Explain why this loss affects skeletal muscle function.

### OUTCOMES 9.4, 9.5, 9.11, 9.13, 9.14

**3.** List four skills encountered in everyday life that depend on nervous system function, and list the part of the nervous system responsible for each.

### OUTCOMES 9.11, 9.13

**4.** The biceps-jerk reflex is carried out by motor neurons that exit the spinal cord in the fifth spinal nerve (C5). The triceps-jerk reflex uses motor neurons in the seventh spinal nerve (C7). Describe how these reflexes might be tested to help pinpoint damage in a patient with a neck injury.

### OUTCOMES 9.11, 9.14

**5.** Describe the roles of the cerebrum and cerebellum in athletics.

### OUTCOMES 9.13, 9.14

**6.** Describe expected functional losses in a patient who has suffered injury to the right occipital lobe of the cerebral cortex compared to injury in the right temporal lobe of the cerebral cortex.

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# 10

# The Senses

*Our appreciation of music involves neurons in the brain sensitive to specific frequencies of sound.*

The sound of music. The band Nirvana and singer Tori Amos have each recorded the song "Smells Like Teen Spirit." In the original Nirvana version, Kurt Cobain's voice is loud and brash, as is the instrumentation; in contrast, Tori Amos's song is slow and subdued. Yet it is easy to tell that these are the same songs. What isn't easy is figuring out how the brain does this.

Some neurons in the auditory cortex sense a certain range of frequencies of incoming sound waves, but others are "pitch-sensitive," which means that they can recognize the same note, whether it comes from an oboe or an elephant. This property of sound, called pitch, is a vibration frequency. The vibration is complex—plucking a string on an instrument vibrates the entire string, but also vibrates parts of it, creating a complex sound. Pitch-sensitive neurons recognize the "fundamental" vibration, which is the lowest one coming from the entire vibrating object, corresponding to plucking the entire string.

In experiments to identify and localize pitch-sensitive neurons, researchers placed electrodes over the auditory cortices of marmoset monkeys, who hear the same range of sounds as humans. When the monkeys listened to sounds that shared the fundamental vibration, even though different sources made the sounds, the same neurons fired action potentials. Moreover, the pitch-sensitive neurons in the monkey brains were in the same part of the auditory cortex that is damaged in humans who lose the ability to distinguish pitches after suffering a stroke. However, we don't yet know how the brain learns and matches the temporal combination of notes that make up a melody—which is how we perceive that Kurt Cobain and Tori Amos sang the same song. Presumably memory is part of the picture, which may explain why we can remember lyrics to a song many years after last hearing it.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

**10.1 Introduction**

1. Distinguish between general senses and special senses. (p. 274)

**10.2 Receptors, Sensations, and Perception**

2. Name five kinds of receptors, and explain their functions. (p. 274)
3. Explain how a sensation arises. (p. 274)

**10.3 General Senses**

4. Describe the receptors associated with the senses of touch, pressure, temperature, and pain. (p. 275)
5. Describe how the sense of pain is produced. (p. 278)

**10.4 Special Senses**

6. Identify the locations of the receptors associated with the special senses. (p. 278)

**10.5 Sense of Smell**

7. Explain the relationship between the senses of smell and taste. (p. 278)
8. Explain the mechanism for smell. (p. 279)

**10.6 Sense of Taste**

9. Explain the mechanism for taste. (p. 280)

**10.7 Sense of Hearing**

10. Explain the function of each part of the ear. (pp. 282–283)

**10.8 Sense of Equilibrium**

11. Distinguish between static and dynamic equilibrium. ( p. 286)

**10.9 Sense of Sight**

12. Explain the function of each part of the eye. (pp. 289–294)
13. Explain how the eye refracts light. (p. 295)
14. Describe the visual nerve pathway. (p. 297)

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## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**choroid** [skinlike] *choroid* coat: Middle, vascular layer of the eye.

**cochlea** [snail] *cochlea:* Coiled tube in the inner ear.

**iris** [rainbow] *iris:* Colored, muscular part of the eye.

**labyrinth** [maze] *labyrinth:* Complex system of connecting chambers and tubes of the inner ear.

**lacri-** [tears] *lacri*mal gland: Tear gland.

**macula** [spot] *macula* lutea: Yellowish spot on the retina.

**olfact-** [to smell] *olfact*ory: Pertaining to the sense of smell.

**scler-** [hard] *scler*a: Tough, outer protective layer of the eye.

**tympan-** [drum] *tympan*ic membrane: Eardrum.

**vitre-** [glass] *vitre*ous humor: Clear, jellylike substance within the eye.

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## 10.1 | Introduction

How dull life would be without sight and sound, smell and taste, touch and balance. Our senses are necessary not only for us to enjoy life, but to survive. They derive from structures called *sensory receptors* that detect environmental changes and trigger impulses that travel on sensory pathways into the central nervous system for processing. The body reacts with a particular feeling or sensation.

Sensory receptors vary greatly, but fall into two major categories. Receptors associated with the *general senses* are widely distributed throughout the skin and deeper tissues, and are structurally simple. Receptors of the second type are parts of complex, specialized sensory organs that provide the *special senses*.

## 10.2 | Receptors, Sensations, and Perception

All action potentials are the same (all-or-none), yet we experience different sensations. Our awareness of different sensory events arises from receptors that respond to specific stimuli and the ability of different parts of the brain to interpret the resulting impulses.

### Types of Receptors

Sensory receptors are diverse but share certain features. Each type of receptor is particularly sensitive to a distinct kind of environmental change and is much less sensitive to other forms of stimulation. Sensory receptors are categorized into five types according to their sensitivities: **Chemoreceptors** (ke″mo-re-sep′torz) are stimulated by changes in the concentration of certain chemicals; **pain receptors** (pān re-sep′torz) by tissue damage; **thermoreceptors** (ther′mo-re-sep′torz) by changes in temperature; **mechanoreceptors** (mek″ah-no-re-sep′torz) by changes in pressure or movement; and **photoreceptors** (fo″to-re-sep′torz) by light.

### Sensations and Perception

A **sensation** occurs when sensory receptors reach threshold and the resulting action potentials cause the brain to become aware of the stimulus. A *perception* occurs when the brain interprets those sensory impulses. Thus, pain is a sensation, but realizing that you have just stepped on a tack is a perception.

At the same time that a sensation forms, the cerebral cortex causes the feeling to seem to come from the stimulated receptors. This process is called **projection** (pro-jek′shun) because the brain projects the sensation back to its apparent source. Projection allows a person to perceive the region of stimulation; this is how the eyes seem to see, and the ears seem to hear.

Because all the impulses that travel away from sensory receptors into the central nervous system are alike, the resulting sensation depends on which region of the brain receives the impulses. For example, impulses reaching one region are always interpreted as sounds, and those reaching another are always perceived as touch. (Some receptors, such as those that measure oxygen levels in the blood, do not trigger sensations.)

### Sensory Adaptation

The brain must prioritize the sensory input it receives, or incoming unimportant information would be overwhelming. For example, until this sentence prompts you to think about it, you are probably unaware of the pressure of your clothing against your skin, or the background noise in the room. This ability of the nervous system to become less responsive to a maintained stimulus is called **sensory adaptation** (ad″ap-ta′shun). It may result from receptors becoming unresponsive or inhibition along the central nervous system pathways leading to the respective sensory regions of the cerebral cortex.

## PRACTICE

1. List five general types of sensory receptors.
2. Explain how a perception is different from a sensation.
3. What is sensory adaptation?

## 10.3 | General Senses

General senses are widespread, and are associated with receptors in the skin, muscles, joints, and viscera. They include the senses of touch and pressure, temperature, and pain.

### Touch and Pressure Senses

The senses of touch and pressure derive from three kinds of receptors (fig. 10.1). These receptors sense mechanical forces that deform or displace tissues. Touch and pressure receptors include:

1. **Free nerve endings** These receptors are common in epithelial tissues, where their free ends branch and extend between epithelial cells. They are responsible for the sensation of itching.
2. **Tactile (Meissner's) corpuscles** These are small, oval masses of flattened connective tissue cells in connective tissue sheaths. Two or more sensory nerve fibers branch into each corpuscle and end in it as tiny knobs.

   Tactile corpuscles are abundant in hairless areas of skin, such as the lips, fingertips, palms, soles, nipples, and external genital organs. They respond to the motion of objects that barely contact the skin, interpreting impulses from them as the sensation of light touch.
3. **Lamellated (Pacinian) corpuscles** These sensory bodies are relatively large structures composed of connective tissue fibers and cells, with a single sensory nerve fiber branch extending into each. They are common in the deeper dermal and subcutaneous tissues and in muscle tendons and joint ligaments. Lamellated corpuscles respond to heavy pressure and are associated with the sensation of deep pressure.

### Temperature Senses

Temperature sensation depends on two types of free nerve endings in the skin. Those that respond to warmer temperatures are called *warm receptors,* and those that respond to colder temperatures are called *cold receptors.*

Warm receptors are most sensitive to temperatures above 25°C (77°F) and become unresponsive at temperatures above 45°C (113°F). Temperatures near and above 45°C also stimulate pain receptors, producing a burning sensation.

Cold receptors are most sensitive to temperatures between 10°C (50°F) and 20°C (68°F). Temperatures below 10°C also stimulate pain receptors, producing a freezing sensation.

Both warm and cold receptors adapt rapidly. Within about a minute of continuous stimulation, the sensation of warmth or cold begins to fade.

### Sense of Pain

Certain receptors that consist of free nerve endings respond to painful stimuli. These receptors are widely distributed throughout the skin and internal tissues, except in the nervous tissue of the brain, which lacks pain receptors.

Pain receptors protect the body because tissue damage stimulates them. Pain sensation is usually perceived as unpleasant, and it signals a person to act to remove the stimulation. Pain receptors adapt very little, if at all (although pathways may be inhibited, as discussed later on page 278). Once a pain receptor is activated, even by a single stimulus, it may send impulses into the central nervous system for some time. Thus, pain may persist.

CAREER CORNER

### Optometrist

The woman squints at the medicine bottle, just barely making out the letters of the label. Since turning 50, she's noticed difficulty reading small print, and she finally acknowledges that she may need glasses. She visits an optometrist, who uses a series of tests to detect the woman's farsightedness. The optometrist assesses visual acuity (reading an eye chart), peripheral vision, color and depth perception, focusing ability, and coordination of the eyes. He also checks for signs of disease, including macular degeneration, glaucoma, cataracts, conjunctivitis, and diabetic retinopathy. The optometrist assures the patient that her eyes are healthy, but eyeglasses or contact lenses will enable her to easily read the fine print.

An optometrist completes four years in optometry school postcollege. Optometrists with advanced training can provide vision therapy (exercises to better coordinate the eyes) and help patients with low vision use devices to supplement lenses and surgery. An optometrist can be the first health-care professional to report a rare syndrome that has ocular symptoms, such as thin retinal layers or abnormal blood vessels.

An optometrist may work with an ophthalmologist to care for a patient before and after a procedure, such as cataract surgery. In some states optometrists can prescribe drugs. Continuing education is very important for optometrists to learn to use new equipment. Optometrists work in private practice and in vision care centers.

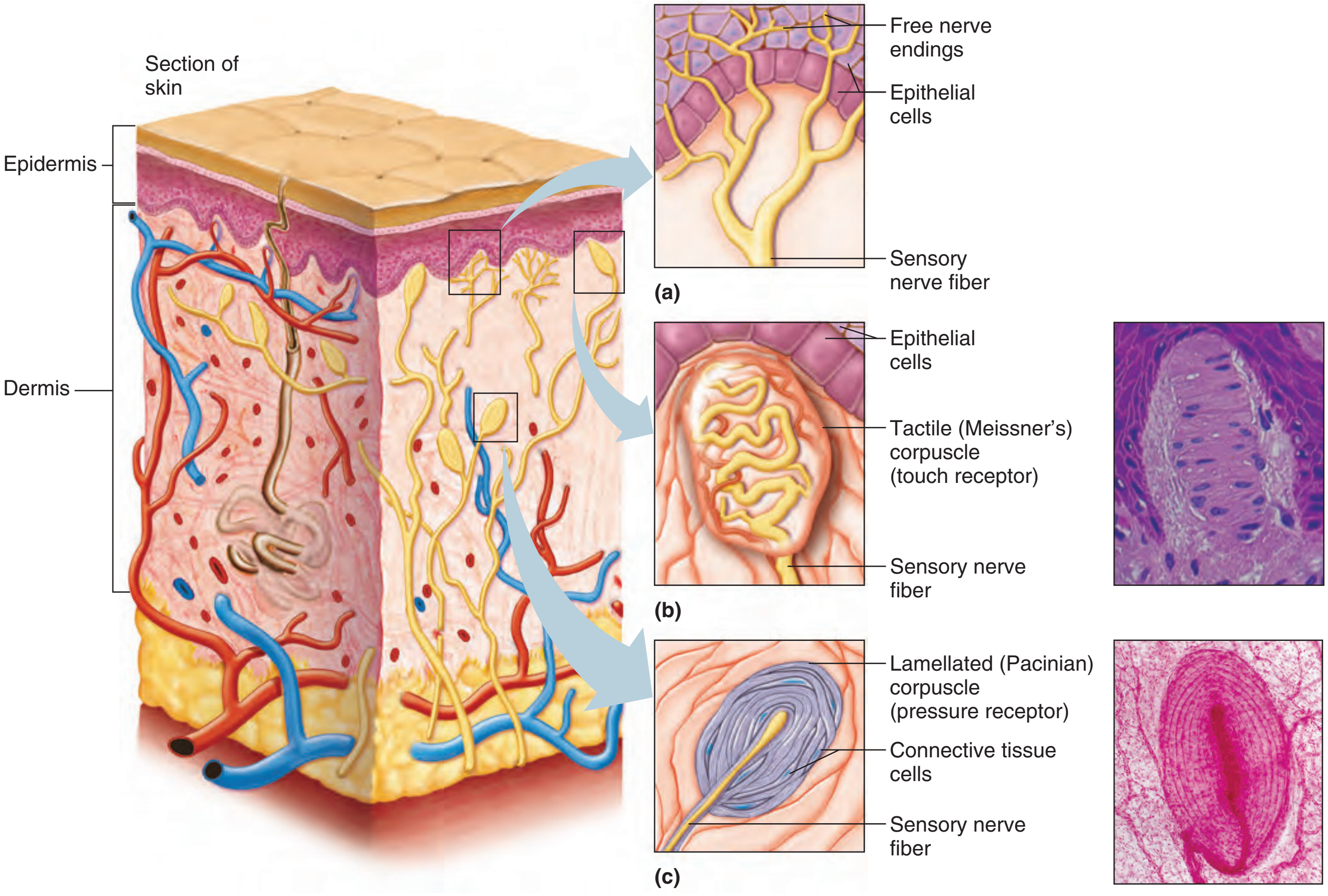


**FIGURE 10.1** APR Touch and pressure receptors include **(a)** free ends of sensory nerve fibers, **(b)** tactile corpuscles (with 225× micrograph), and **(c)** lamellated corpuscles (with 50× micrograph).

The way in which tissue damage stimulates pain receptors is poorly understood. Injuries likely promote the release of certain chemicals that build up and stimulate pain receptors. A deficiency of oxygen-rich blood (hypoxia) or disruption of blood flow (ischemia) in a tissue triggers pain sensations. For example, the pain elicited during a muscle cramp stems from sustained contraction that squeezes capillaries and interrupts blood flow, allowing pain-stimulating chemicals to accumulate. Stimulation of mechanical-sensitive pain receptors also contributes to the sensation.

Injuries to bones, tendons, or ligaments stimulate pain receptors that may also trigger contraction of nearby skeletal muscles. The contracting muscles may become ischemic, which may stimulate still other pain receptors.

### *Visceral Pain*

As a rule, pain receptors are the only receptors in viscera whose stimulation produces sensations. Pain receptors in these organs respond differently to stimulation than those associated with surface tissues. For example, localized damage to intestinal tissue during surgical procedures may not elicit pain sensations, even in a conscious person. However, when visceral tissues are subjected to more widespread stimulation, such as when intestinal tissues are stretched or smooth muscle in intestinal walls undergo a spasm, a strong pain sensation may follow. Once again, the resulting pain seems to stem from stimulation of mechanoreceptors and from decreased blood flow accompanied by lower tissue oxygen concentration and accumulation of pain-stimulating chemicals via chemoreceptors.

Visceral pain may feel as if it is coming from a part of the body other than the part being stimulated, a phenomenon called **referred pain.** For example, pain originating in the heart may be referred to the left shoulder or left upper limb (fig. 10.2). Referred pain may arise from common nerve pathways that conduct sensory impulses from skin areas as well as viscera. Pain impulses from the heart travel over the same nerve pathways as those from the skin of the left shoulder and left upper limb (fig. 10.3). Consequently, during a heart attack, the cerebral cortex may incorrectly interpret the source of the pain impulses as the left shoulder or upper limb, rather than the heart.

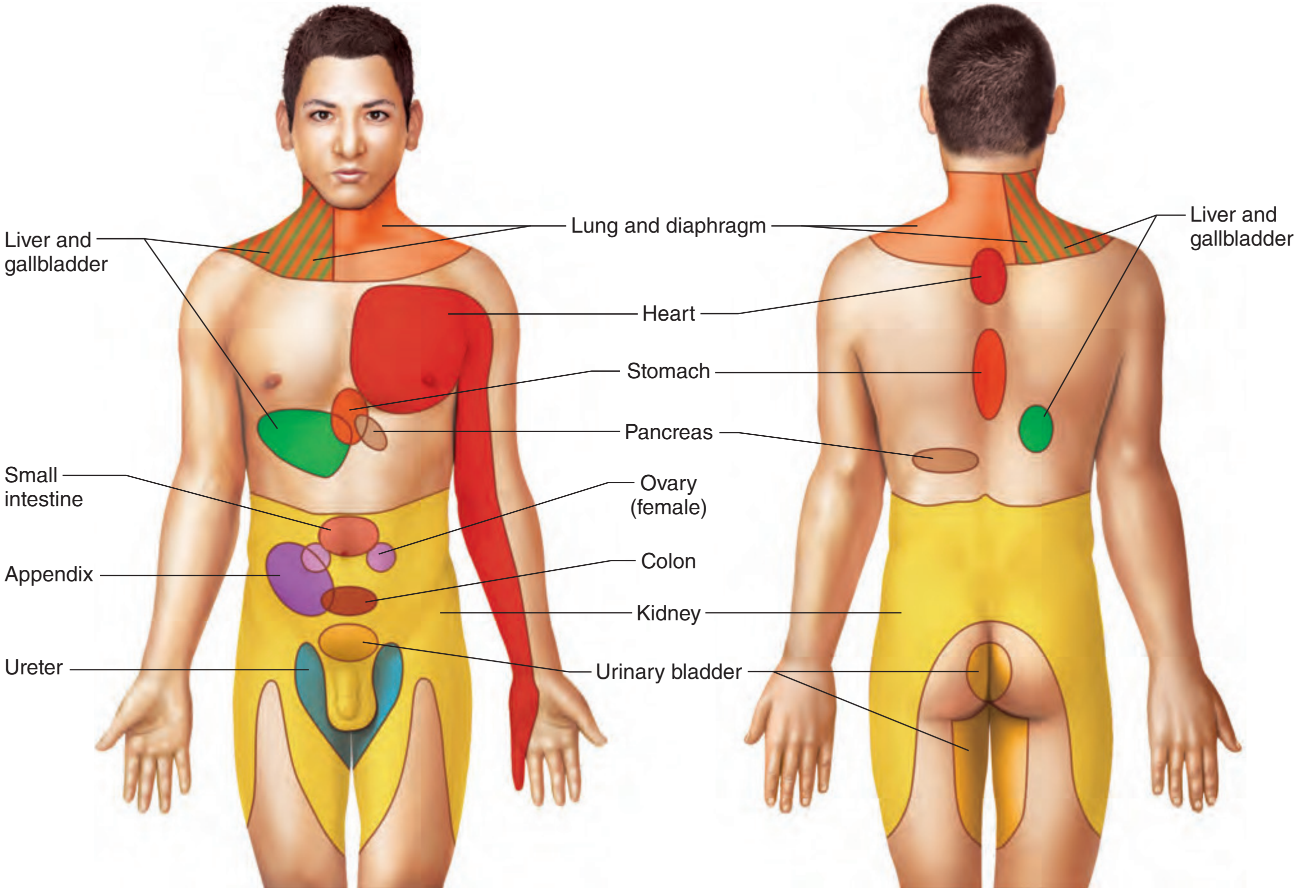

Liver and gallbladder
Lung and diaphragm
Liver and gallbladder
Heart
Stomach
Pancreas
Small intestine
Ovary (female)
Appendix
Colon
Kidney
Ureter
Urinary bladder

**FIGURE 10.2** Referred pain feels as if it is coming from a different body part than the one being stimulated. Visceral pain may be felt at the surface regions indicated in the illustration.

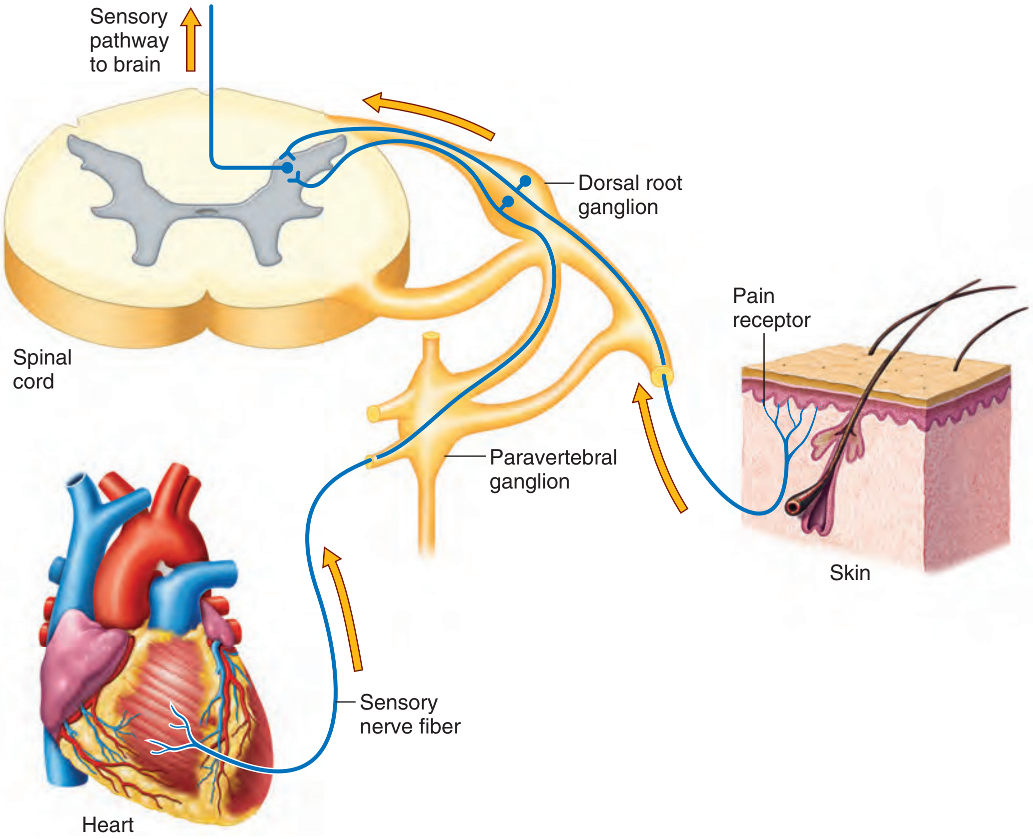

Sensory pathway to brain
Dorsal root ganglion
Pain receptor
Spinal cord
Paravertebral ganglion
Skin
Sensory nerve fiber
Heart

**FIGURE 10.3** Pain originating in the heart may feel as if it is coming from the skin because sensory impulses from the heart and the skin follow common nerve pathways to the brain.

**PRACTICE**

4. Describe the three types of touch and pressure receptors.
5. Describe the receptors that sense temperature.
6. What types of stimuli excite pain receptors?
7. What is referred pain?

### *Pain Nerve Fibers*

The fibers (axons) that conduct impulses away from pain receptors are of two main types: acute pain fibers and chronic pain fibers. *Acute pain fibers* are myelinated. They conduct impulses rapidly and are associated with the sensation of sharp pain, which typically originates from a restricted area of the skin and seldom continues after the pain-producing stimulus stops. *Chronic pain fibers* are unmyelinated. They conduct impulses more slowly and produce a dull, aching sensation that may be diffuse and difficult to pinpoint. Such pain may continue for some time after the original stimulus ceases. Acute pain is usually sensed as coming only from the skin; chronic pain is felt in deeper tissues as well.

An event that stimulates pain receptors usually triggers impulses on both acute and chronic pain fibers. This causes a dual sensation—a sharp, pricking pain, followed shortly by a dull, aching one. The aching pain is usually more intense and may worsen with time. Chronic pain can cause prolonged suffering.

Pain impulses that originate from the head reach the brain on sensory fibers of cranial nerves. All other pain impulses travel on the sensory fibers of spinal nerves, and they pass into the spinal cord by way of the dorsal roots of these spinal nerves. Within the spinal cord, neurons process pain impulses in the gray matter of the dorsal horn, and the impulses are conducted to the brain. Here, most pain fibers terminate in the reticular formation (see chapter 9, p. 255). From there, other neurons conduct impulses to the thalamus, hypothalamus, and cerebral cortex.

### *Regulation of Pain Impulses*

Awareness of pain arises when pain impulses reach the thalamus—that is, even before they reach the cerebral cortex. The cerebral cortex, however, determines pain intensity, locates the pain source, and mediates emotional and motor responses to the pain.

Areas of gray matter in the midbrain, pons, and medulla oblongata regulate movement of pain impulses from the spinal cord. Impulses from special neurons in these brain areas descend in the lateral funiculus (see chapter 9, p. 246) to various levels of the spinal cord. These impulses stimulate the ends of certain nerve fibers to release biochemicals that can block pain signals by inhibiting presynaptic nerve fibers in the posterior horn of the spinal cord.

The inhibiting substances released in the posterior horn include neuropeptides called *enkephalins* and the biogenic amine *serotonin* (see chapter 9, p. 239). Enkephalins can suppress acute and chronic pain impulses and thus can relieve severe pain, much as morphine and other opiate drugs do. In fact, enkephalins bind to the same receptor sites on neuron membranes as does morphine. Serotonin stimulates other neurons to release enkephalins.

*Endorphins* are another group of neuropeptides with pain-suppressing, morphinelike actions. Endorphins are found in the pituitary gland and the hypothalamus. Enkephalins and endorphins are released in response to extreme pain and provide natural pain control.

Children who have *hereditary sensory and autonomic neuropathy* cannot feel pain, and as a result they inadvertently injure themselves. More common is *peripheral neuropathy*, in which the hands and/or feet become numb due to too few tactile corpuscles. In one study, people with normal pain sensation had an average of 12 corpuscles per square millimeter of skin, whereas people with peripheral neuropathy had fewer than 3. The most common causes of peripheral neuropathy are diabetes mellitus, cancer treatment, vitamin deficiency, and HIV infection.

**PRACTICE**

8. Describe two types of pain fibers.
9. How do acute pain and chronic pain differ?
10. What parts of the brain interpret pain impulses?
11. How do neuropeptides help control pain?

## 10.4 | Special Senses

Special senses are those whose sensory receptors are in large, complex sensory organs in the head. These senses and their respective organs include the following:

- Smell → Olfactory organs
- Taste → Taste buds
- Hearing ┐
- Equilibrium ┘ → Ears
- Sight → Eyes

Clinical Application 10.1 describes a condition in which some of these assignments of senses to sense organs are altered.

## 10.5 | Sense of Smell

The sense of smell is associated with complex sensory structures in the upper region of the nasal cavity.

### Olfactory Receptors

Smell (olfactory) receptors and taste receptors are chemoreceptors, which means that chemicals dissolved in liquids stimulate them. Smell and taste function closely

### CLINICAL APPLICATION 10.1

## Synesthesia: Connected Senses

*"The song was full of glittering orange diamonds."*
*"The paint smelled blue."*
*"The sunset was salty."*
*"The pickle tasted like a rectangle."*

About 1 in 2,000 people have a condition called synesthesia ("joined sensation"), in which sensation and perception mix, so that the brain perceives a stimulus to one sense as coming from another. Most commonly, letters, numbers, or periods of time evoke specific colors. These associations are involuntary, are very specific, and persist over a lifetime. For example, a person might report that 3 is always mustard yellow, or Thursday a very dark, shiny brown.

Synesthesia runs in families, and geneticists have associated the condition with inheriting variants in any of four different genes. Female "synesthetes" outnumber males six to one. Creative individuals are overrepresented among those with the condition. They include musicians Syd Barrett, John Mayer, Tori Amos, and Franz Liszt, architect Frank Lloyd Wright, and physicist Richard Feynman, who used to include the hues with which he visualized chemical equations on the chalkboard, to the amusement of his students. One of the coauthors of this book has it—to her, days are colors. The earliest recorded mention of synesthesia is an essay from John Locke in 1690. More and more people with synesthesia are recognizing that their peculiar talent has a name, thanks to Internet groups devoted to the condition.

Researchers hypothesize that mixed senses are present in all babies, but synesthesia develops in individuals who do not "prune" as many synapses as others as they age. (A loss of 20 billion synapses a day is normal for adults.) Imaging studies and animal experiments have localized the neurons that convey synesthetic connections to the general area where the temporal, parietal, and occipital lobes meet. Once sometimes referred to as a learning disability, synesthesia is instead now increasingly viewed as an enhancement to learning—and a fuller way of enjoying our sensual worlds.

together and aid in food selection because we usually smell food at the same time we taste it.

## Olfactory Organs

The **olfactory organs,** which contain the olfactory receptor cells, are yellowish-brown masses of epithelium about the size of postage stamps that cover the upper parts of the nasal cavity, the superior nasal conchae, and a part of the nasal septum. **Olfactory receptor cells** are bipolar neurons surrounded by columnar epithelial cells (fig. 10.4). Hairlike cilia cover tiny knobs at the distal ends of these neurons' dendrites. In any particular such neuron, the cilia harbor many copies of one type of olfactory receptor membrane protein. Chemicals called odorant molecules stimulate various sets of olfactory receptor proteins, and therefore various sets of olfactory receptor cells, to send a signal of

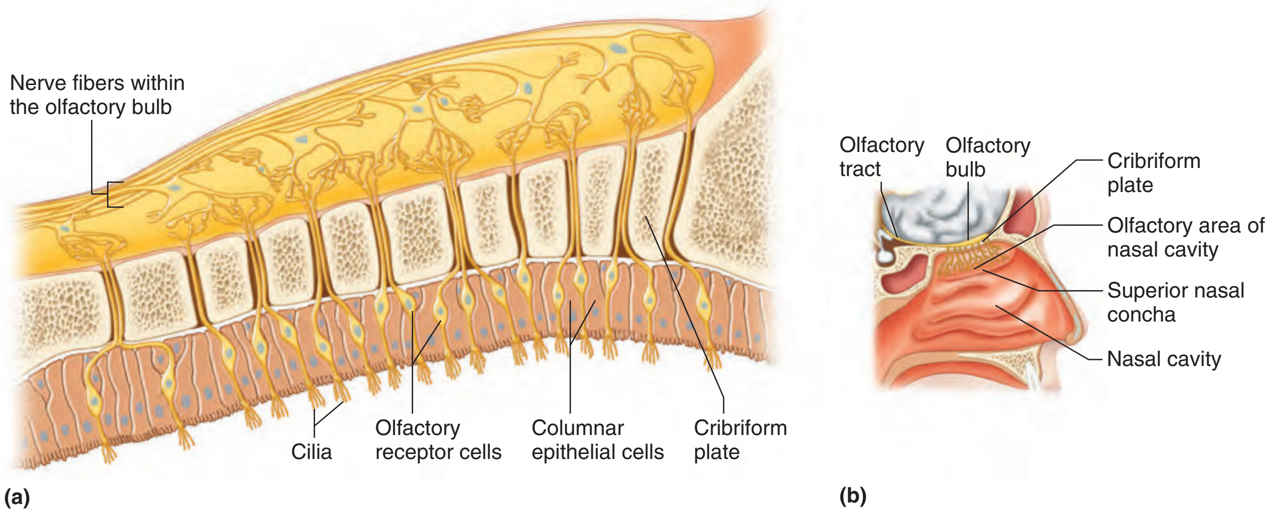


**FIGURE 10.4** APR Olfactory receptors convey the sense of smell. **(a)** Columnar epithelial cells support olfactory receptor cells, which have cilia at their distal ends. The actual olfactory receptors, which are proteins, are on the cilia. Binding of odorants to these receptors in distinctive patterns conveys the information that the brain interprets as an odor. **(b)** The olfactory area is associated with the superior nasal concha.

a detected odor to the brain. Odorant molecules enter the nasal cavity, but must dissolve at least partially in the watery fluids that surround the cilia before receptors can detect them. Foods, flowers, and many other things release odorant molecules.

## Olfactory Pathways

Stimulated olfactory receptor cells send impulses along their axons. These axons (which together form the first pair of cranial nerves) synapse with neurons located in enlargements called **olfactory bulbs.** These structures lie on either side of the crista galli of the ethmoid bone (see fig. 7.14, p. 158). In the olfactory bulbs the impulses are analyzed, and as a result additional impulses are conducted along the **olfactory tracts**. The major interpreting areas for these impulses in the olfactory cortex lie within the temporal lobes and at the bases of the frontal lobes, anterior to the hypothalamus. Impulses conducted on the olfactory tract also reach the limbic system (see chapter 9, p.254), which is responsible for any emotional response to an odor.

Canines' excellent sense of smell is the basis of using service dogs to detect impending health problems in their owners. The dogs sense subtle odors that people emit when becoming ill in certain ways. Service dogs are used to sense imminent seizures, drops in blood glucose and heart rate, and lung, breast, and thyroid cancers. Experiments confirm that dogs are especially sensitive to odorant molecules on the skin or in the sweat of sick people.

## Olfactory Stimulation

When odorant molecules bind to olfactory receptor proteins in olfactory receptor cell membranes, a biochemical pathway is activated that culminates in a depolarizing influx of sodium ions, which may trigger an action potential if the depolarization reaches threshold. The action potentials from this and other olfactory receptor cells travel to the olfactory bulbs in the brain, where the sensation of smell arises.

The several hundred types of olfactory receptor cells can code for many thousands of odors when they signal the brain in groups. That is, an odorant molecule stimulates a distinct set of receptor types. An olfactory receptor cell has only one type of olfactory receptor, but that receptor can bind several types of odorant molecules. In addition, any one odorant molecule can bind several types of receptors. The brain interprets this binding information as a combinatorial olfactory code. In a simplified example, if there are ten odor receptors, parsley might stimulate receptors 3, 4, and 8, while chocolate might stimulate receptors 1, 5, and 10. Researchers identify olfactory and taste receptors by searching human genome sequence information for proteins that reside in cell membranes and are produced only in certain receptor cells. A person may have to sniff and force air up to the receptor areas to smell a faint odor because the olfactory organs are high in the nasal cavity above the usual pathway of inhaled air. Astronauts on the first space flights reportedly could not smell their food because they had to squeeze the food from tubes directly into their mouths—odorant molecules were not inhaled as they usually are.

The sense of smell adapts rapidly, but adaptation to one scent will not diminish sensitivity to new odors. For example, a person visiting a fish market might at first be acutely aware of the fishy smell, but then that odor fades. If a second person enters the fish market wearing a strong perfume, the person already there, who has become accustomed to the stinky fish, will nonetheless detect the flowery scent of the perfume.

Partial or complete loss of smell is called *anosmia*. It may result from inflammation of the nasal cavity lining due to a respiratory infection, tobacco smoking, or using certain drugs, such as cocaine.

**PRACTICE**

12. Where are olfactory receptors located?
13. Trace the pathway of an olfactory impulse from a receptor to the cerebrum.

## 10.6 | Sense of Taste

**Taste buds** are the special organs of taste (fig. 10.5). The 10,000 or so taste buds are located primarily on the surface of the tongue and are associated with tiny elevations called *papillae*. About 1,000 taste buds are scattered in the roof of the mouth and walls of the throat.

### Taste Receptors

Each taste bud includes 50 to 150 modified epithelial cells which function as receptor cells, the **taste cells** (gustatory cells). Each taste cell is replaced on average every ten days. The taste bud also includes epithelial supporting cells. The entire structure is spherical, with an opening, the **taste pore,** on its free surface. Tiny projections called **taste hairs** protrude from the outer ends of the taste cells and extend from the taste pore. These taste hairs are the sensitive parts of the receptor cells.

Interwoven among the taste cells and wrapped around them is a network of sensory fibers. Stimulation of a receptor cell triggers an impulse on a nearby fiber, and the impulse then travels into the brain.

**FACTS OF LIFE** Our varied taste sensations may help us stay healthy. Sweet tastes direct us to energy-providing carbohydrates, sour tastes compel us to avoid foods containing dangerous acids, salty foods entice us to eat sodium, bitter tastes help us avoid poisons, and savory umami taste sensations increase our protein intake.

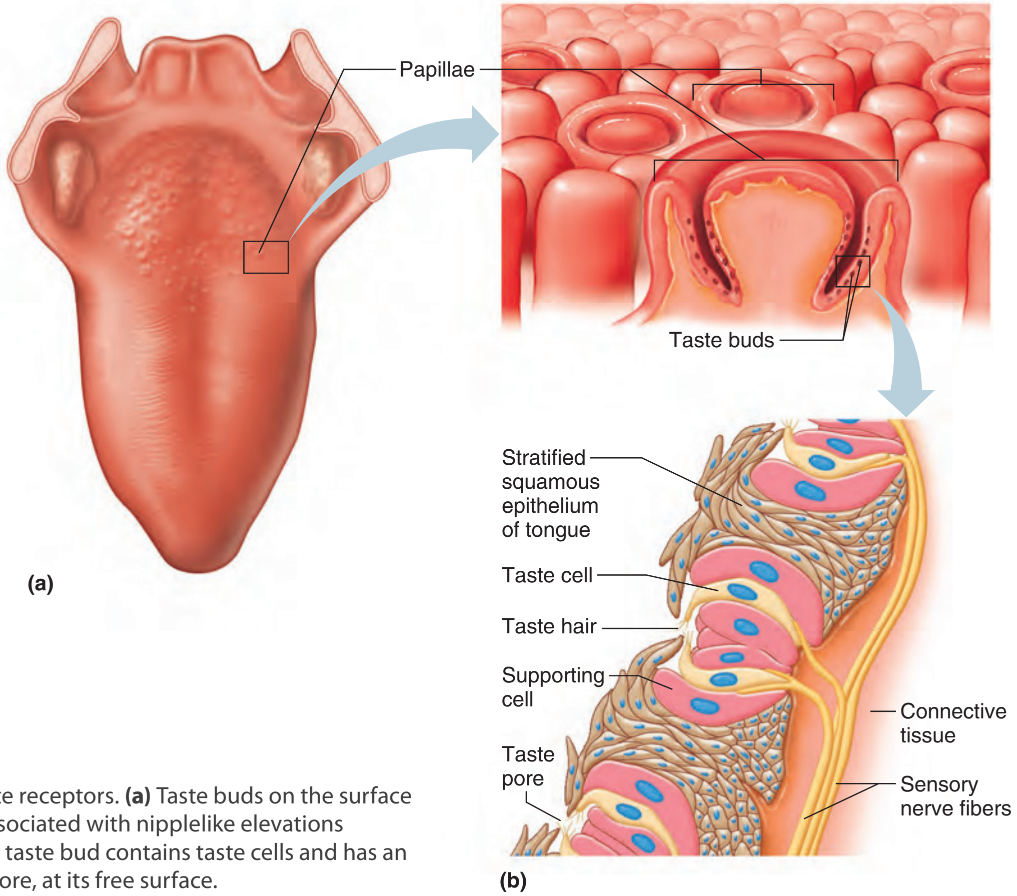


**FIGURE 10.5** Taste receptors. **(a)** Taste buds on the surface of the tongue are associated with nipplelike elevations called papillae. **(b)** A taste bud contains taste cells and has an opening, the taste pore, at its free surface.

A particular chemical must dissolve in the watery fluid surrounding the taste buds in order for it to be tasted. The salivary glands provide this fluid. Food molecules bind to specific receptor proteins embedded in taste hairs on the taste cells. The pattern of receptor types that bind food molecules and generate impulses on nearby sensory fibers is interpreted as a particular taste sensation. Therefore, the chemical senses of smell and taste arise from molecules from the environment that bind membrane receptors on neurons specialized as sensory receptors.

The taste cells in all taste buds appear alike microscopically, but are of at least five types. Each type is most sensitive to a particular kind of chemical stimulus, producing at least five primary taste (gustatory) sensations.

## Taste Sensations

The five primary taste sensations are:

1. *Sweet,* such as table sugar
2. *Sour,* such as a lemon
3. *Salty,* such as table salt
4. *Bitter,* such as caffeine or quinine
5. *Umami* (a Japanese term meaning “delicious”), a response to certain amino acids and their chemical relatives, such as monosodium glutamate (MSG).

Some investigators recognize other taste sensations—*alkaline* and *metallic.*

A flavor results from one or a combination of the primary sensations. Experiencing flavors involves tasting, which reflects the concentrations of stimulating chemicals, as well as smelling and feeling the texture and temperature of foods. Furthermore, the chemicals in some foods—chili peppers and ginger, for instance—may stimulate pain receptors, which cause a burning sensation. In fact, the chemical in chili peppers that tastes “hot”—capsaicin—actually stimulates heat receptors.

Experiments indicate that each taste cell responds to one taste sensation only, with distinct receptors. Taste cells for each of the five taste sensations are in all areas of the tongue, but are distributed such that each sensation seems to arise most strongly from a particular region. The tip of the tongue is most sensitive to sweet stimuli, the margins of the tongue most sensitive to sour, the back of the tongue more likely to detect bitter substances, and responsiveness to salt quite widely distributed.

Taste sensation, like the sense of smell, undergoes adaptation rapidly. Moving bits of food over the surface of the tongue to stimulate different receptors at different moments keeps us from losing taste due to sensory adaptation.

## Taste Pathways

Sensory impulses from taste receptor cells in the tongue travel on fibers of the facial, glossopharyngeal, and vagus nerves into the medulla oblongata. From there, the impulses ascend to the thalamus and are directed to the gustatory cortex, in the parietal lobe of the cerebrum, along a deep part of the lateral sulcus (see fig. 9.29, p. 251).

**PRACTICE**

14. Why is saliva necessary for the sense of taste?
15. Name the five primary taste sensations.
16. Trace a sensory impulse from a taste receptor to the cerebral cortex.

## 10.7 | Sense of Hearing

The organ of hearing, the ear, has outer, middle, and inner parts. The ear also functions in the sense of equilibrium.

### Outer (External) Ear

The outer ear consists of three parts. The first is an outer, funnel-like structure called the **auricle** (aw′ri-kl) or pinna. The second is an S-shaped tube called the **external acoustic meatus** (me-a′tus), or external auditory canal, that leads inward through the temporal bone for about 2.5 centimeters (fig. 10.6). The meatus terminates with the third part, the **eardrum** or tympanic membrane.

The transmission of vibrations through matter produces sound. Vibrating strings or reeds produce the sounds of some musical instruments, and vibrating vocal folds in the larynx produce the voice. The auricle of the ear helps collect sound waves traveling through the air and directs them into the external acoustic meatus. At the end of the meatus, the sound waves reach the eardrum.

The eardrum is a semitransparent membrane covered by a thin layer of skin on its outer surface and by mucous membrane on the inside. It has an oval margin and is cone-shaped, with the apex of the cone directed inward. The attachment of one of the auditory ossicles (the malleus) maintains the eardrum's cone shape. Sound waves that enter the external acoustic meatus change the pressure on the eardrum, which moves back and forth in response and thus reproduces the vibrations of the sound-wave source.

### Middle Ear

The middle ear, or *tympanic cavity,* is an air-filled space in the temporal bone. It contains three small bones called **auditory ossicles** (aw′di-to″re os′i-klz): the *malleus,* the *incus,* and the *stapes* (fig. 10.7). Tiny ligaments attach them to the wall of the tympanic cavity, and they are covered by mucous membrane. These bones bridge the eardrum and the inner ear, transmitting vibrations between these parts. Specifically, the malleus attaches to the eardrum, and when the eardrum vibrates, the malleus vibrates in unison. The malleus causes the incus to vibrate, and the incus passes the movement on to the stapes. Ligaments hold the stapes to an opening in the wall of the tympanic cavity called the **oval window,** which leads into the inner ear. Vibration of the stapes at

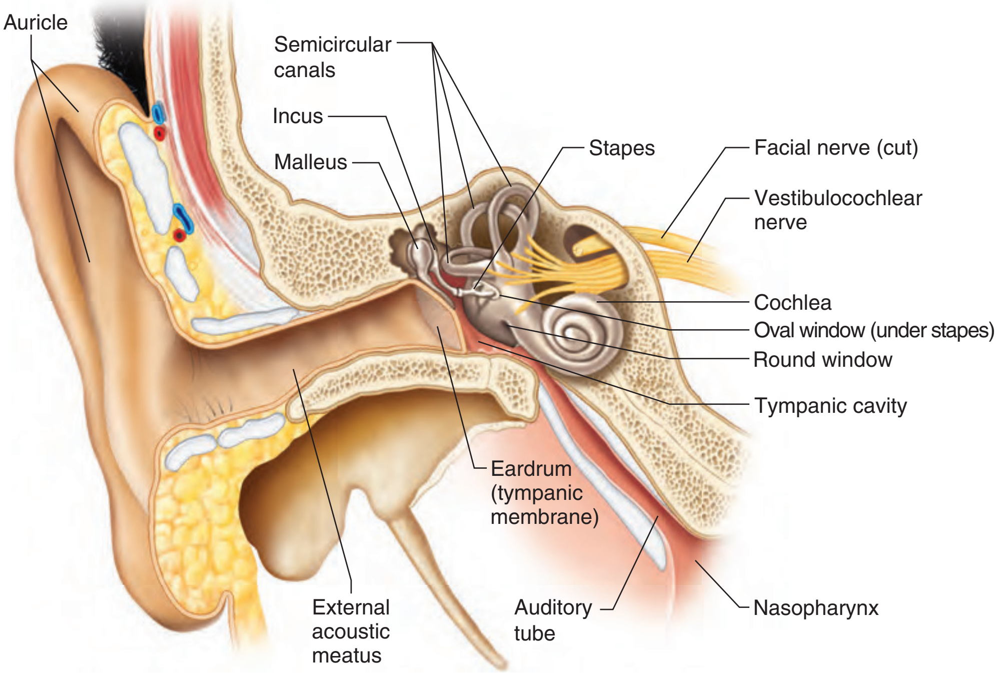


**FIGURE 10.6** APR Major parts of the ear. The outer ear includes the auricle, external acoustic meatus, and eardrum. The middle ear includes the auditory ossicles (malleus, incus, and stapes) and the oval window. The inner ear includes the semicircular canals and the cochlea.

Q *Which cranial bone is shown in this figure?*

**Answer can be found in Appendix F on page 582.**

the oval window moves a fluid in the inner ear, which stimulates the hearing receptors.

The auditory ossicles help increase (amplify) the force of vibrations as they pass from the eardrum to the oval window, in addition to transmitting vibrations. The vibrational force concentrates as it moves from the outer to the inner ear because the ossicles transmit vibrations from the relatively large surface of the eardrum to a much smaller area at the oval window. As a result, the pressure (per square millimeter) that the stapes applies on the oval window is many times greater than the pressure that sound waves exert on the eardrum.

## Auditory Tube

An **auditory tube** (aw′di-to″re tūb) or eustachian tube connects each middle ear to the back of the nasal cavity (nasopharynx). This tube conducts air between the tympanic cavity and the outside of the body by way of the nose and mouth. The auditory tube helps maintain equal air pressure on both sides of the eardrum, which is necessary for normal hearing.

The function of the auditory tube is noticeable during rapid changes in altitude. As a person moves from a higher altitude to a lower one, air pressure on the outside of the eardrum increases. This may push the eardrum inward, impairing hearing. When the air pressure difference is great enough, air movement through the auditory tube equalizes the pressure on both sides of the eardrum, and the membrane moves back into its regular position. This produces a popping sound, which restores normal hearing.

Mucous membrane infections of the throat may spread through the auditory tubes and cause middle ear infection because auditory tube mucous membranes connect directly with middle ear linings. Pinching a nostril when blowing the nose may force material from the throat up the auditory tube and into the middle ear.

## Inner (Internal) Ear

The inner ear is a complex system of communicating chambers and tubes called a **labyrinth** (lab′ĭ-rinth). Each ear has two parts to the labyrinth—the *osseous labyrinth* and the *membranous labyrinth* (fig. 10.8). The osseous labyrinth is a bony canal in the temporal bone. The membranous labyrinth is a tube of similar shape that lies within the osseous labyrinth. Between the osseous and membranous labyrinths is a fluid called *perilymph,* which is secreted by cells in the wall of the bony canal. The membranous labyrinth contains another fluid, called *endolymph.*

The parts of the labyrinths include three **semicircular canals,** which provide a sense of equilibrium (discussed in section 10.8 on pp. 286–287, and a **cochlea** (kok′le-ah), which functions in hearing. The cochlea has a bony core and a thin, bony shelf that winds around the core like the threads of a screw. The shelf divides the osseous labyrinth of the cochlea into upper and lower compartments. The upper compartment, called the *scala vestibuli,* leads from the oval window to the apex of the spiral. The lower compartment, the *scala tympani,* extends from the apex of the cochlea to a membrane-covered opening in the wall of the inner ear called the **round window** (fig. 10.8).

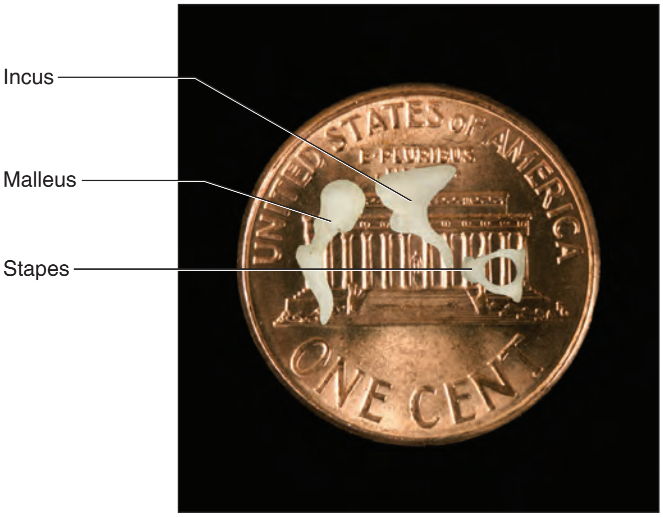


**FIGURE 10.7** The auditory ossicles—the malleus, incus, and stapes—are bones that bridge the eardrum and the inner ear (2.5×). Comparison to a penny emphasizes their tiny size.

The part of the membranous labyrinth within the cochlea is called the *cochlear duct.* It lies between the two bony compartments and ends as a closed sac at the apex of the cochlea. The cochlear duct is separated from the scala vestibuli by a *vestibular membrane* (Reissner's membrane) and from the scala tympani by a *basilar membrane* (fig. 10.9).

The basilar membrane has many thousands of stiff, elastic fibers, which lengthen from the base of the cochlea to its apex. Sound vibrations entering the perilymph at the oval window travel along the scala vestibuli and pass through the vestibular membrane and into the endolymph of the cochlear duct, where they move the basilar membrane.

After passing through the basilar membrane, the vibrations enter the perilymph of the scala tympani. Their forces are dissipated into the air in the tympanic cavity by movement of the membrane covering the round window.

The **spiral organ** (organ of Corti) contains the hearing receptors. It is located on the upper surface of the basilar membrane and stretches from the apex to the base of the cochlea (fig. 10.9). The receptor cells, called *hair cells,* are organized in rows and have many hairlike processes that project into the endolymph of the cochlear duct. Above these hair cells is a *tectorial membrane* attached to the bony shelf of the cochlea, passing over the receptor cells and contacting the tips of their hairs.

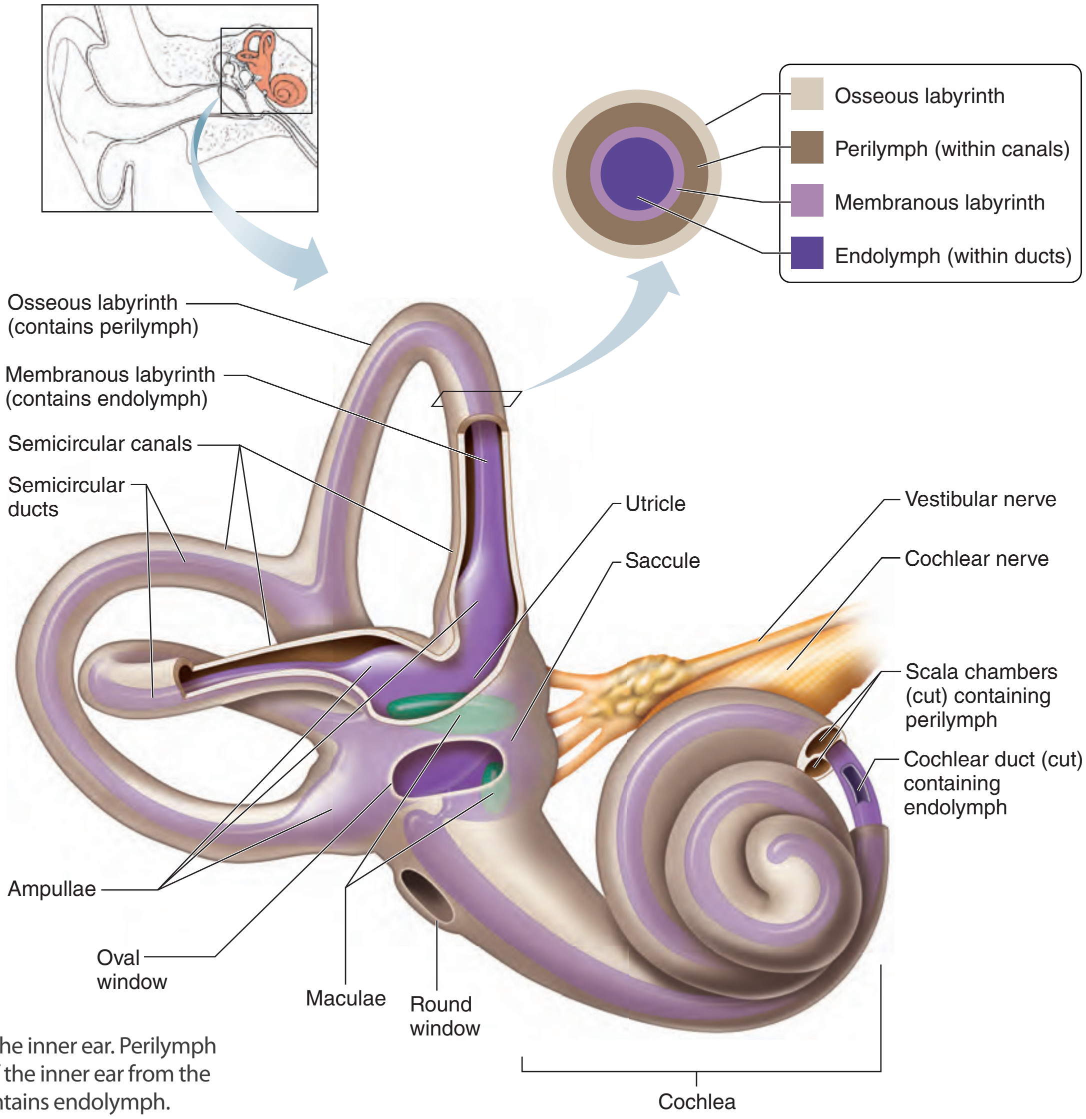

Osseous labyrinth
Perilymph (within canals)
Membranous labyrinth
Endolymph (within ducts)
Osseous labyrinth (contains perilymph)
Membranous labyrinth (contains endolymph)
Semicircular canals
Semicircular ducts
Utricle
Saccule
Vestibular nerve
Cochlear nerve
Scala chambers (cut) containing perilymph
Cochlear duct (cut) containing endolymph
Ampullae
Oval window
Maculae
Round window
Cochlea

**FIGURE 10.8** A closer look at the inner ear. Perilymph separates the osseous labyrinth of the inner ear from the membranous labyrinth, which contains endolymph.

As sound vibrations pass through the inner ear, the hairs shear back and forth against the tectorial membrane, and the resulting mechanical deformation of the hairs stimulates the hair cells (figs. 10.9 and 10.10). Different hair cells have different sensitivities to the frequency (pitch) of sound waves. This enables us to hear sounds of different pitch simultaneously.

Hair cells are epithelial, but function somewhat like neurons. For example, when a hair cell is at rest, its membrane is polarized. When it is stimulated, selective ion channels open, depolarizing the membrane and making it more permeable to calcium ions. The hair cell has no axon or dendrites, but it has neurotransmitter-containing vesicles near its base. As calcium ions diffuse into the cell, some of these vesicles fuse with the cell membrane and release neurotransmitter by exocytosis. The neurotransmitter stimulates the ends of nearby sensory neurons, and in response they conduct action potentials along the cochlear branch of the vestibulocochlear nerve to the auditory cortex of the temporal lobe of the brain.

The ear of a young person with normal hearing can detect sound waves with frequencies ranging from 20 to 20,000 or more vibrations per second. The range of greatest sensitivity is 2,000–3,000 vibrations per second. Table 10.1 summarizes the steps of hearing.

Recall from chapter 9 (pp. 238–239) that action potentials are all-or-none. More-intense stimulation of the hair cells causes more action potentials per second to reach the auditory cortex, and we sense a louder sound.

Units called *decibels* (dB) measure sound intensity on a logarithmic scale. The decibel scale begins at 0 dB, which is the intensity of the sound that is least perceptible by a normal human ear. A sound of 10 dB is 10 times as intense as the least perceptible sound; a sound of 20 dB is 100 times as intense; and a sound of 30 dB is 1,000 times as intense. A whisper has an intensity of about 40 dB, normal conversation measures 60–70 dB, and heavy traffic produces about 80 dB. A sound of 120 dB, common at a rock concert, produces discomfort, and a sound of 140 dB, such as that emitted by a jet plane at takeoff, causes pain. Frequent or prolonged exposure to sounds with intensities above 85 dB can damage hearing receptors and cause permanent hearing loss.

## Auditory Pathways

The nerve fibers associated with hearing enter the auditory pathways, which pass into the auditory cortices of the temporal lobes of the cerebrum, where they are interpreted. On the way, some of these fibers cross over, so that impulses arising from each ear are interpreted on both sides of the brain. Consequently, damage to a temporal lobe on one side of the brain does not necessarily cause complete hearing loss in the ear on that side.

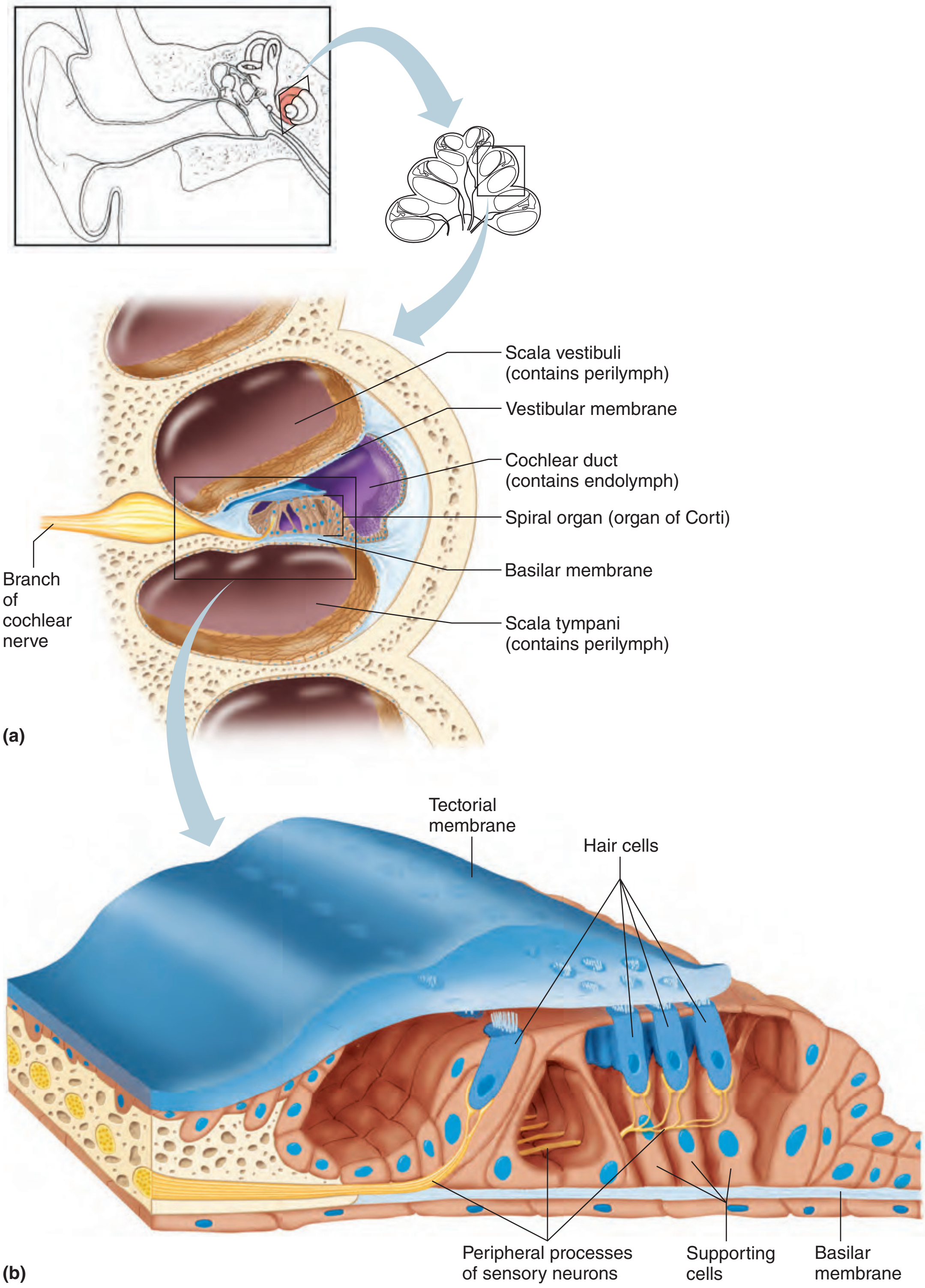

Scala vestibuli (contains perilymph)
Vestibular membrane
Cochlear duct (contains endolymph)
Spiral organ (organ of Corti)
Basilar membrane
Scala tympani (contains perilymph)
Branch of cochlear nerve
(a)
Tectorial membrane
Hair cells
Peripheral processes of sensory neurons
Supporting cells
Basilar membrane
(b)

**FIGURE 10.9** APR The cochlea. **(a)** Cross section of the cochlea. **(b)** The spiral organ and the tectorial membrane.

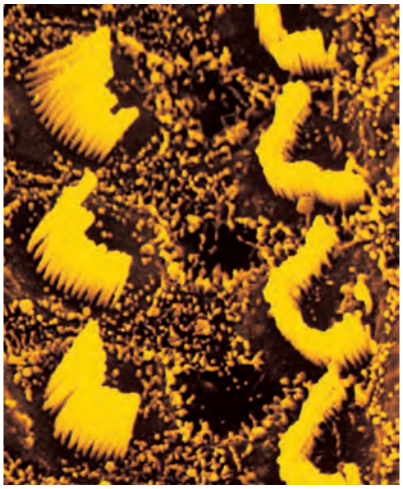


**FIGURE 10.10** Scanning electron micrograph of hair cells in the spiral organ (3,800×).

Several factors cause partial or complete hearing loss. Interference with the transmission of vibrations to the inner ear is called *conductive hearing loss*. Conductive hearing loss may be due to plugging of the external acoustic meatus or to changes in the eardrum or auditory ossicles. For example, the eardrum may harden as a result of disease and become less responsive to sound waves, or disease or injury may tear or perforate the eardrum.

Damage to the cochlea, auditory nerve, or auditory pathways can cause *sensorineural hearing loss*. Sensorineural hearing loss can be caused by loud sounds, tumors in the central nervous system, brain damage as a result of vascular accidents, or use of certain drugs.

| TABLE 10.1 | Steps in the Generation of Sensory Impulses from the Ear |
|---|---|
| 1. | Sound waves enter external acoustic meatus. |
| 2. | Waves of changing pressures cause eardrum to reproduce vibrations coming from sound wave source. |
| 3. | Auditory ossicles amplify and transmit vibrations to end of stapes. |
| 4. | Movement of stapes at oval window transmits vibrations to perilymph in scala vestibuli. |
| 5. | Vibrations pass through the vestibular membrane and enter endolymph of cochlear duct. |
| 6. | Different frequencies of vibration in endolymph stimulate different sets of receptor cells. |
| 7. | As a receptor cell depolarizes, its membrane becomes more permeable to calcium ions. |
| 8. | Inward diffusion of calcium ions causes vesicles at the base of the receptor cell to release neurotransmitter. |
| 9. | Neurotransmitter stimulates ends of nearby sensory neurons. |
| 10. | Sensory impulses are triggered on fibers of the cochlear branch of vestibulocochlear nerve. |
| 11. | Auditory cortices of temporal lobes interpret sensory impulses. |

## PRACTICE

17. How are sound waves transmitted through the outer, middle, and inner ears?
18. Distinguish between the osseous and membranous labyrinths.
19. Describe the spiral organ.

## 10.8 | Sense of Equilibrium

The sense of equilibrium is really two senses—static equilibrium and dynamic equilibrium—that come from different sensory organs. The organs of **static equilibrium** (stat′ik e″kwĭ-lib′re-um) sense the position of the head, maintaining stability and posture when the head and body are still. When the head and body suddenly move or rotate, the organs of **dynamic equilibrium** (di-nam′ik e″kwĭ-lib′re-um) detect such motion and aid in maintaining balance.

### Static Equilibrium

The organs of static equilibrium are in the **vestibule,** a bony chamber between the semicircular canals and the cochlea. The membranous labyrinth inside the vestibule consists of two expanded chambers—a **utricle** (u′trĭ-kl) and a **saccule** (sak′ūl) (see fig. 10.8).

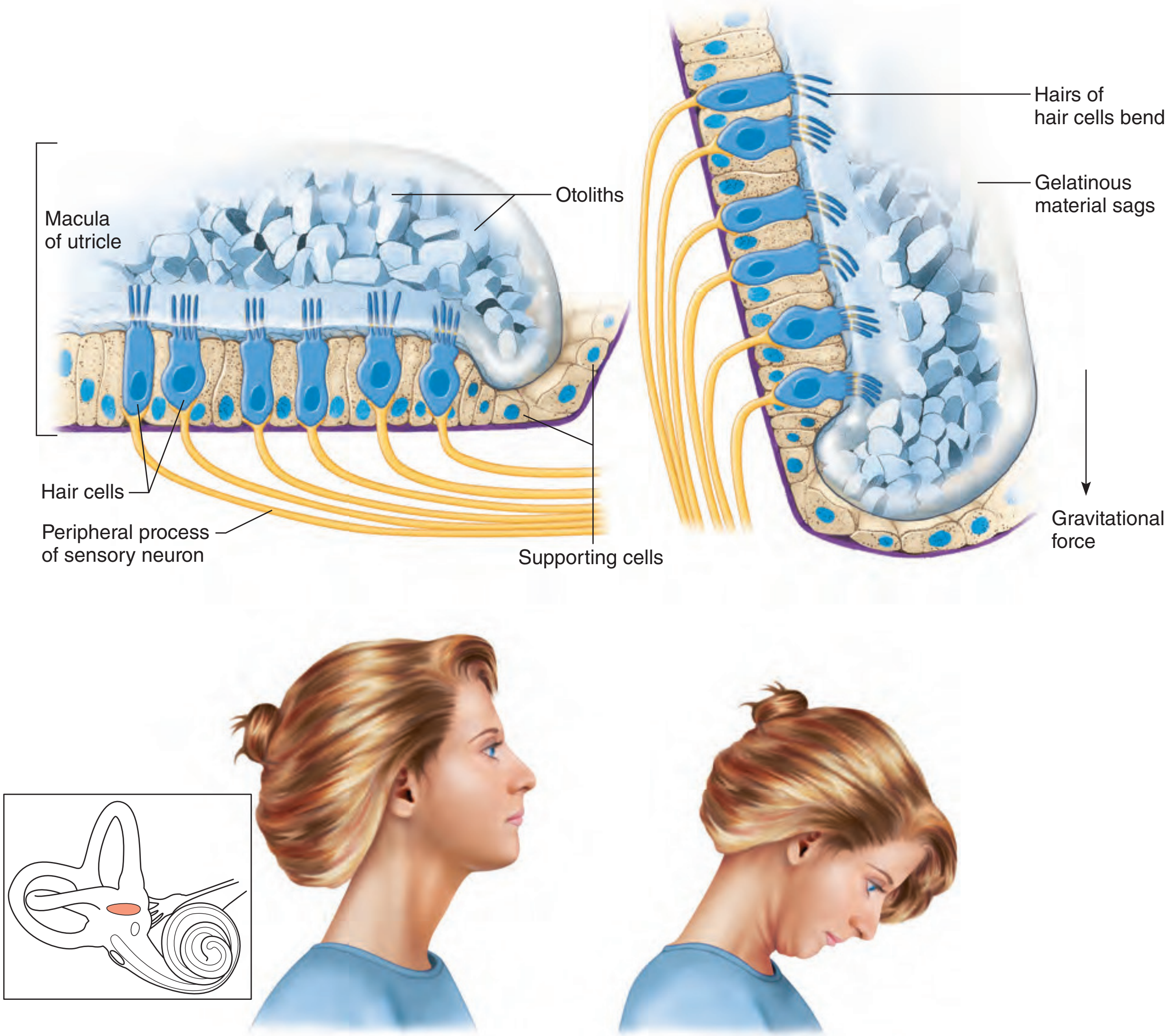
The saccule and utricle each have a tiny structure called a **macula** (mak′u-lah). Maculae have many hair cells, which serve as sensory receptors. The hairs of the hair cells project into a mass of gelatinous material, which has grains of calcium carbonate (otoliths) embedded in it. These particles add weight to the gelatinous structure.

The head bending forward, backward, or to one side stimulates hair cells. Such movements tilt the gelatinous masses of the maculae, and as they sag in response to gravity, the hairs projecting into them bend. This action stimulates the hair cells, and they signal the neurons associated with them in a manner similar to that of hearing receptors. The resulting action potentials are conducted into the central nervous system on the vestibular branch of the vestibulocochlear nerve, informing the brain of the head's new position. The brain responds by sending motor impulses to skeletal muscles, which contract or relax to maintain balance (fig. 10.11).

### Dynamic Equilibrium

The organs of dynamic equilibrium are the three semicircular canals in the labyrinth. They detect motion of the head and aid in balancing the head and body during sudden movement. These canals lie at right angles to each other (see fig. 10.8).

Suspended in the perilymph of the osseous portion of each semicircular canal is a membranous semicircular duct that ends in a swelling called an **ampulla**



**(a) Head upright** **(b) Head bent forward**

**FIGURE 10.11** The maculae respond to changes in head position. **(a)** Macula of the utricle with the head in an upright position. **(b)** Macula of the utricle with the head bent forward.

(am-pul′ah), which houses the sensory organs of the semicircular canals. Each of these organs, called a **crista ampullaris** (kris′tah am-pul′ar-is), contains a number of sensory hair cells and supporting cells (fig. 10.12). Like the hairs of the maculae, the hair cells extend upward into a dome-shaped, gelatinous mass called the *cupula*.

Rapid turns of the head or body stimulate the hair cells of the crista ampullaris (fig. 10.13). At such times, the semicircular canals move with the head or body, but the fluid inside the membranous ducts remains stationary. This bends the cupula in one or more of the canals in a direction opposite that of the head or body movement, and the hairs embedded in it also bend. The stimulated hair cells signal their associated neurons, which conduct impulses to the brain. The brain interprets these impulses as a movement in a particular direction.

Parts of the cerebellum are particularly important in interpreting impulses from the semicircular canals. Analysis of such information allows the brain to predict the consequences of rapid body movements, and by modifying signals to appropriate skeletal muscles, the cerebellum can maintain balance.

Other sensory structures aid in maintaining equilibrium. For example, certain mechanoreceptors (proprioceptors), particularly those associated with the joints of the neck, inform the brain about the position of body parts. In addition, the eyes detect changes in position that result from body movements. Such visual information is so important that even if the organs of equilibrium are damaged, a person may be able to maintain normal balance by keeping the eyes open and moving slowly.

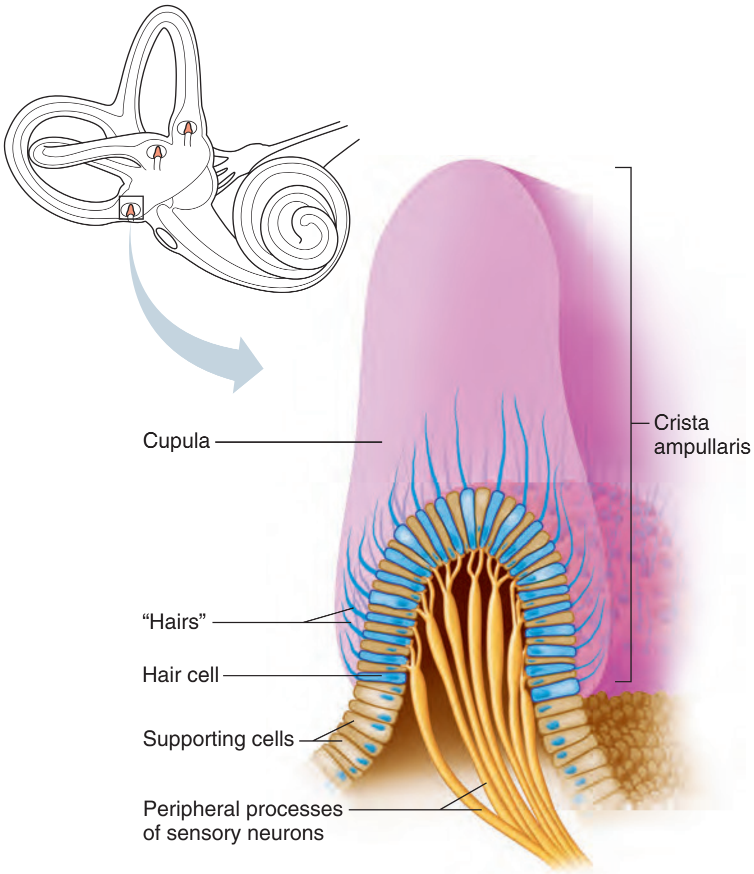

Cupula
Crista ampullaris
"Hairs"
Hair cell
Supporting cells
Peripheral processes of sensory neurons

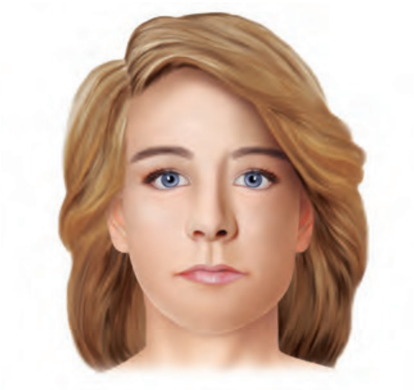
**FIGURE 10.12** A crista ampullaris is located within the ampulla of each semicircular canal.

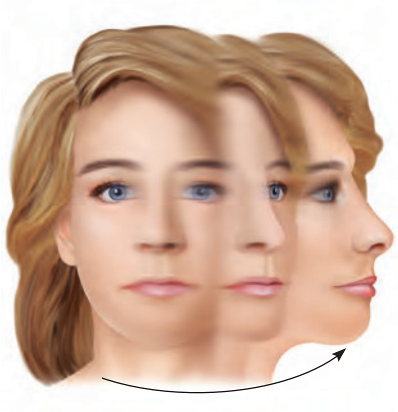
The nausea, vomiting, dizziness, and headache of *motion sickness* arise from sensations that don't make sense. The eyes of a person reading in a moving car, for example, signal the brain that the person is stationary, because the print doesn't move. However, receptors in the skin detect bouncing, swaying, starting and stopping, as the inner ear detects movement. The contradiction triggers the symptoms. Similarly, in a passenger of an airplane flying through heavy turbulence, receptors in the skin and inner ear register the chaos outside, but the eyes focus on the immobile seats and surroundings.

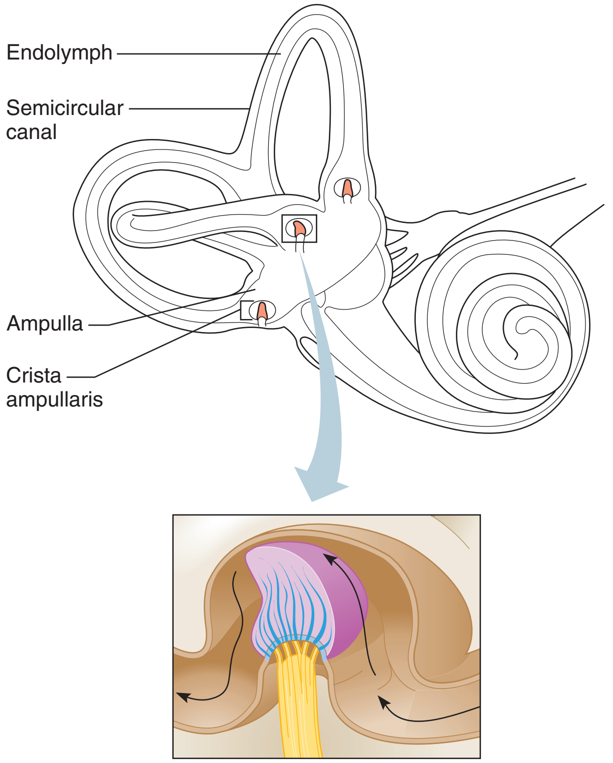
To prevent or lessen the misery of motion sickness, focus on the horizon or an object in the distance ahead. Medications are available by pill (diphenhydramine and meclizine) and, for longer excursions, in a skin patch (scopalamine).

## PRACTICE

20. Distinguish between static and dynamic equilibrium.
21. Which structures provide the sense of static equilibrium? Of dynamic equilibrium?
22. How does sensory information from other receptors help maintain equilibrium?


**(a) Head in still position**


**(b) Head rotating**


Endolymph
Semicircular canal
Ampulla
Crista ampullaris

**(c)**

**FIGURE 10.13** Equilibrium. **(a)** When the head is stationary, the cupula of the crista ampullaris remains upright. **(b)** and **(c)** When the head is moving rapidly, the cupula bends opposite the motion of the head, stimulating sensory receptors.

## 10.9 | Sense of Sight

The eye, the organ containing visual receptors, provides vision, with the assistance of *accessory organs*. These accessory organs include the eyelids and lacrimal apparatus, which protect the eye, and a set of extrinsic muscles, which move the eye.

### Visual Accessory Organs

The eye, lacrimal gland, and associated extrinsic muscles are housed in the orbital cavity, or orbit, of the skull. Each orbit is lined with the periosteum of various bones, and also contains fat, blood vessels, nerves, and connective tissues.

Each **eyelid** has four layers—skin, muscle, connective tissue, and conjunctiva. The skin of the eyelid, which is the thinnest skin of the body, covers the lid's outer surface and fuses with its inner lining near the margin of the lid. The eyelids are moved by the *orbicularis oculi* muscle (see fig. 8.17*a*, p. 207), which acts as a sphincter and closes the lids when it contracts, and by the *levator palpebrae superioris* muscle, which raises the upper lid and thus helps open the eye (fig. 10.14). The **conjunctiva** is a mucous membrane that lines the inner surfaces of the eyelids and folds back to cover the anterior surface of the eyeball, except for its central portion (cornea).

The *lacrimal apparatus* consists of the **lacrimal gland,** which secretes tears, and a series of ducts that carry tears into the nasal cavity (fig. 10.15). The gland is located in the orbit and secretes tears continuously. The tears exit through tiny tubules and flow downward and medially across the eye.

Two small ducts (the superior and inferior canaliculi) collect tears, which flow into the *lacrimal sac,* located in a deep groove of the lacrimal bone, and then into the *nasolacrimal duct,* which empties into the nasal cavity. Secretion by the lacrimal gland moistens and lubricates the surface of the eye and the lining of the lids. Tears also have an enzyme (*lysozyme*) that kills bacteria, reducing the risk of eye infections.

The **extrinsic muscles** arise from the bones of the orbit and insert by broad tendons on the eye's tough outer surface. Six extrinsic muscles move the eye in different directions. Any given eye movement may utilize more than one extrinsic muscle, but each muscle is associated with one primary action. Figure 10.16 illustrates the locations of these extrinsic muscles, and table 10.2 lists their functions, as well as the functions of the eyelid muscles.

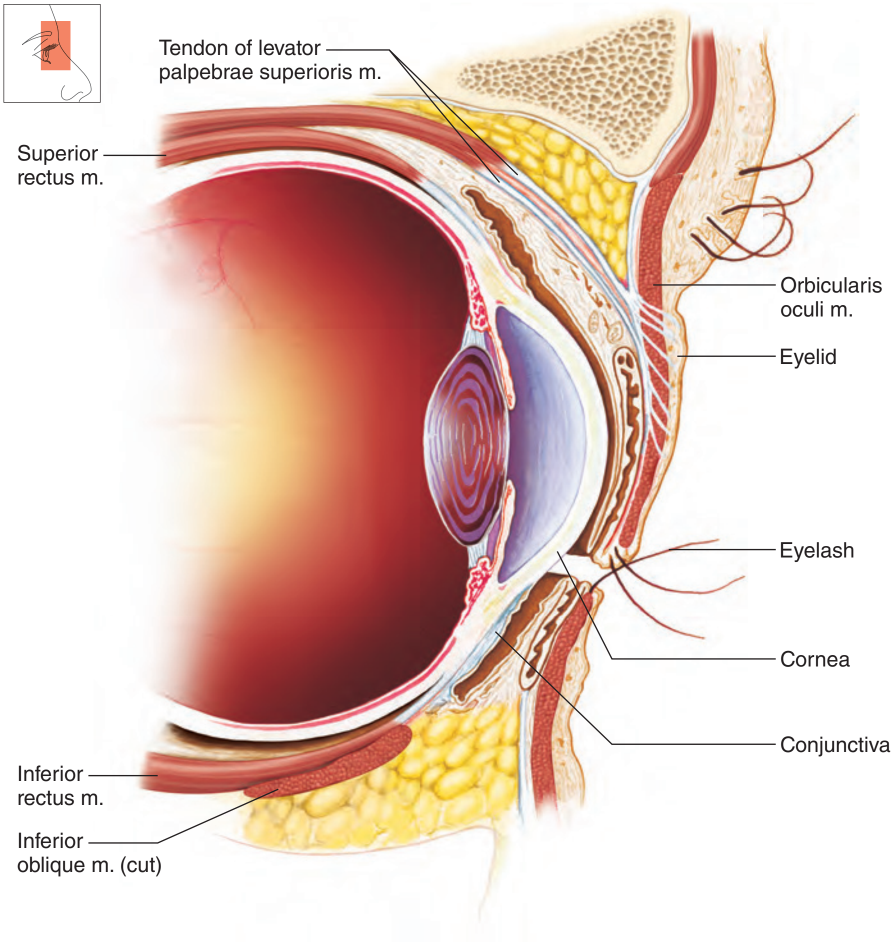


**FIGURE 10.14** Sagittal section of the closed eyelids and anterior portion of the eye.

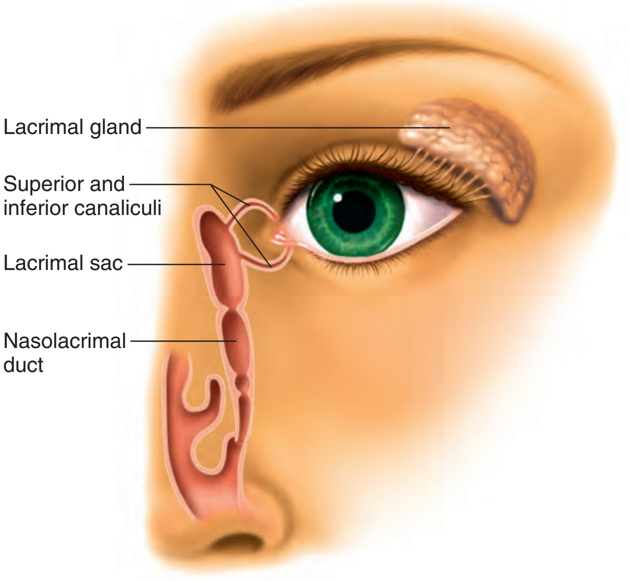


**FIGURE 10.15** The lacrimal apparatus consists of a tear-secreting gland and a series of ducts.

One eye deviating from the line of vision may result in double vision (diplopia). If this condition persists, the brain may suppress the image from the deviated eye. As a result, the turning eye may become blind (suppression amblyopia). Treating eye deviation early in life with exercises, eyeglasses, and surgery can prevent such monocular (one-eye) blindness.

## PRACTICE

23. Explain how the eyelid moves.
24. Describe the conjunctiva.
25. What is the function of the lacrimal apparatus?

## Structure of the Eye

The eye is a hollow, spherical structure about 2.5 centimeters in diameter. Its wall has three distinct layers—an outer (fibrous) layer, a middle (vascular) layer, and an inner (nervous) layer. The spaces within the eye are filled with fluids that support its wall and internal parts that help maintain its shape. Figure 10.17 shows the major parts of the eye.

### *Outer Layer*

The anterior sixth of the outer layer bulges forward as the transparent **cornea** (kor′ne-ah), which is the window of the eye and helps focus entering light rays. The cornea is composed largely of connective tissue with a thin surface layer of epithelium. It is transparent because it contains few cells and no blood vessels, and the cells and collagenous fibers form unusually regular patterns.

The cornea is continuous with the **sclera** (skle′rah), the white portion of the eye. The sclera makes up the posterior five-sixths of the outer layer and is opaque due to many large, disorganized, collagen and elastic fibers. The sclera protects the eye and is an attachment for the extrinsic muscles. In the back of the eye, the **optic nerve** and certain blood vessels pierce the sclera. Clinical Application 10.2 describes headaches that include visual symptoms.

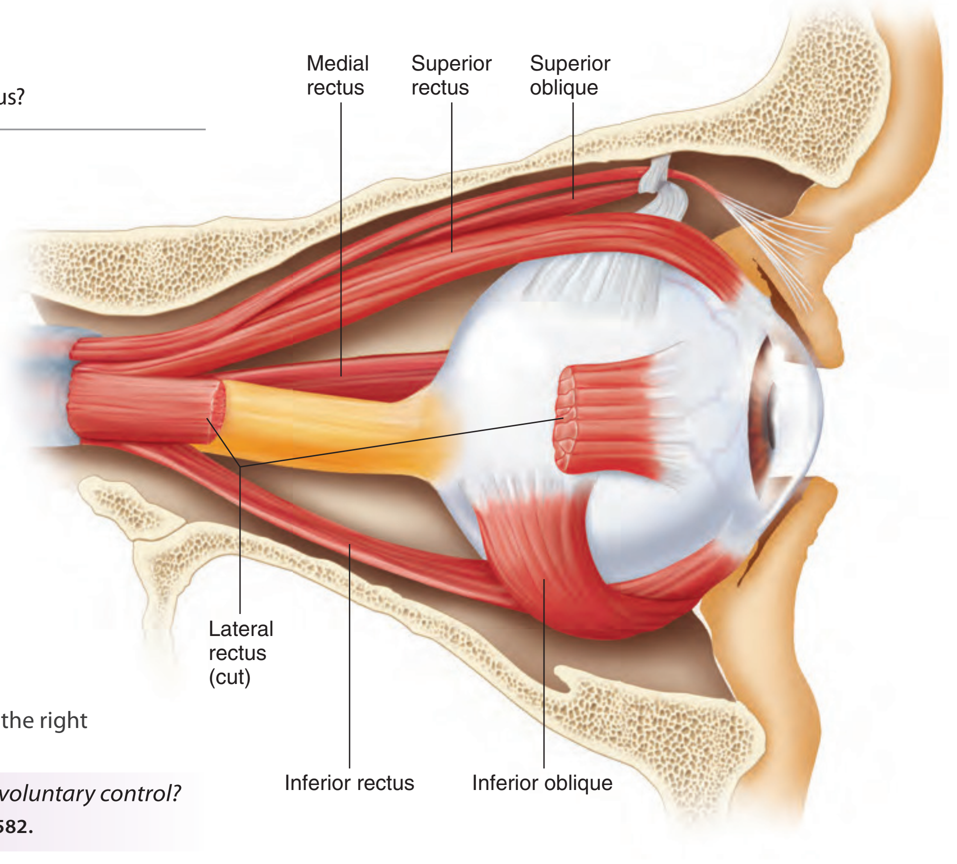


**FIGURE 10.16** APR Extrinsic muscles of the right eye (lateral view).

Q *Are the extrinsic muscles of the eye under voluntary control?*
**Answer can be found in Appendix F on page 582.**

**TABLE 10.2** Muscles Associated with the Eyelids and Eyes

| Name | Innervation | Function |
|---|---|---|
| *Muscles of the Eyelids* | | |
| Orbicularis oculi | Facial nerve (VII) | Closes eye |
| Levator palpebrae superioris | Oculomotor nerve (III) | Opens eye |
| *Extrinsic Muscles of the Eyes* | | |
| Superior rectus | Oculomotor nerve (III) | Rotates eye upward and toward midline |
| Inferior rectus | Oculomotor nerve (III) | Rotates eye downward and toward midline |
| Medial rectus | Oculomotor nerve (III) | Rotates eye toward midline |
| Lateral rectus | Abducens nerve (VI) | Rotates eye away from midline |
| Superior oblique | Trochlear nerve (IV) | Rotates eye downward and away from midline |
| Inferior oblique | Oculomotor nerve (III) | Rotates eye upward and away from midline |

Worldwide, the most common cause of blindness is loss of transparency of the cornea. Each year, 40,000 corneal transplants are performed in the United States. Corneas are "immune privileged," not evoking an immune response, so anyone can donate to anyone. However, corneal transplants are effective only if the transplanted tissue includes stem cells normally found in a layer of cells, called the limbus, which separates the cornea from the conjunctiva. (The cornea itself does not contain stem cells.) Researchers performed limbal cell transplants on patients with corneal damage in one eye. They took the stem cells from the patients' healthy eyes, culturing the limbal cells into a bluish, translucent gel, which they then applied to the affected eyes. Vision returned. Limbal stem cell transplants may prove to be more effective than corneal transplants, which have been done since 1905.

### *Middle Layer*

The middle layer of the wall of the eye includes the choroid coat, ciliary body, and iris (fig. 10.17). The **choroid coat** (ko′roid kōt), in the posterior five-sixths of the globe of the eye, is loosely joined to the sclera and is honeycombed with blood vessels, which nourish surrounding tissues. The choroid coat also has many pigment-producing melanocytes. The melanin that these cells produce absorbs excess light, which helps keep the inside of the eye dark.

The **ciliary body** (sil′e-er″e bod′e), which is the thickest part of the middle layer, extends forward from the choroid coat and forms an internal ring around the front of the eye. Within the ciliary body are many radiating folds called *ciliary processes* and groups of muscle fibers that constitute the *ciliary muscles.*

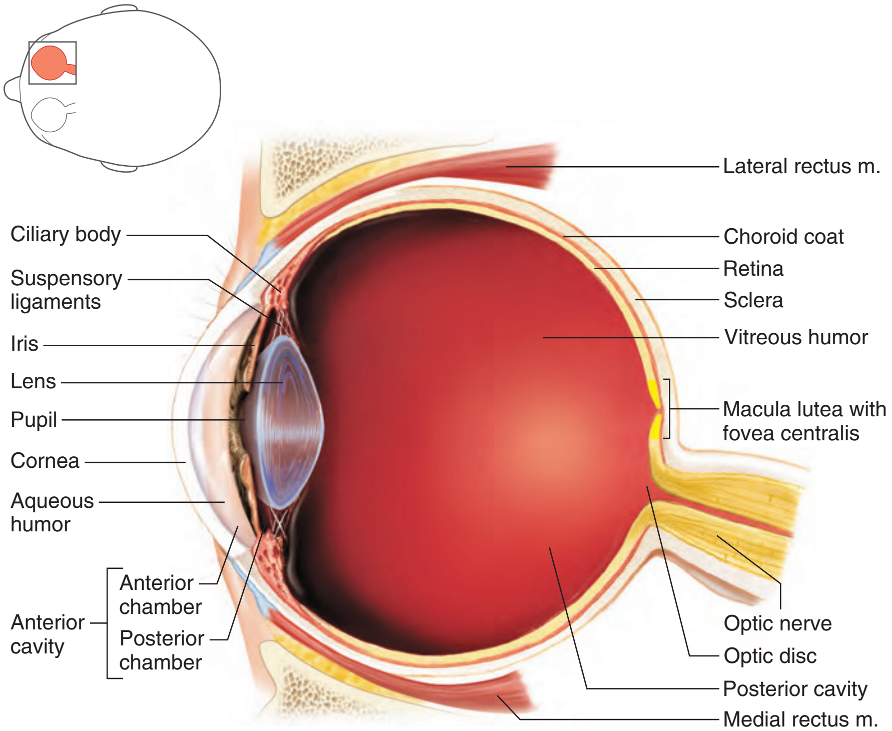

Lateral rectus m.
Ciliary body
Choroid coat
Suspensory ligaments
Retina
Sclera
Iris
Vitreous humor
Lens
Macula lutea with fovea centralis
Pupil
Cornea
Aqueous humor
Anterior chamber
Anterior cavity
Posterior chamber
Optic nerve
Optic disc
Posterior cavity
Medial rectus m.

**FIGURE 10.17** APR Transverse section of the right eye (superior view).

## CLINICAL APPLICATION 10.2

## Headache

Headaches are common. The cells of the nervous tissue in the brain lack pain receptors, but nearly all the other tissues of the head, including the meninges and blood vessels, are richly innervated, and can be the source of headache pain.

Many a *migraine* sufferer knows that an attack is imminent early in the morning, when an ominous dull throbbing begins, often on one side of the head. Migraine is more than head pain—the person feels unwell in a general sense, and an attack can be disabling, lasting from a few hours to several days. In a migraine, certain cranial blood vessels constrict, producing a localized cerebral blood deficiency. When vasodilation quickly follows, a severe headache results. Several types of drugs, such as the triptans, effectively relieve migraines, but they are best taken at the first sign of illness, and several drugs may need to be tried to find an effective one. For some people, keeping a diary of conditions before an attack can reveal a trigger, such as eating chocolate or exposure to low-pressure weather systems.

In some individuals, migraine begins with an "aura" of shimmery bright lights in the peripheral vision. Accompanying the aura is often "photophobia," which is head pain when exposed to light. Photophobia arises from a group of brain neurons closely associated with the optic nerve (see figure 10.26). Completely blind migraine sufferers, whose optic nerves do not function, do not experience photophobia. But people who are "legally blind," with partially degenerated retinas but intact and functional optic nerves, do experience pain from light. Experiments on animals localized neurons near the optic nerve that trigger photophobia when stimulated.

Many headaches are associated with stressful life situations that cause fatigue, emotional tension, anxiety, or frustration. These conditions can trigger various physiological changes, such as prolonged contraction of the skeletal muscles in the forehead, sides of the head, or back of the neck, which stimulate pain receptors and produce a *tension headache.* More severe *vascular headaches* accompany constriction or dilation of the cranial blood vessels. For example, the throbbing headache of a "hangover" from drinking too much alcohol may be due to blood pulsating through dilated cranial vessels. Other causes of headaches include sensitivity to food additives, high blood pressure, increased intracranial pressure due to a tumor or to blood escaping from a ruptured vessel, decreased cerebrospinal fluid pressure following a lumbar puncture, and sensitivity to or withdrawal from certain drugs.

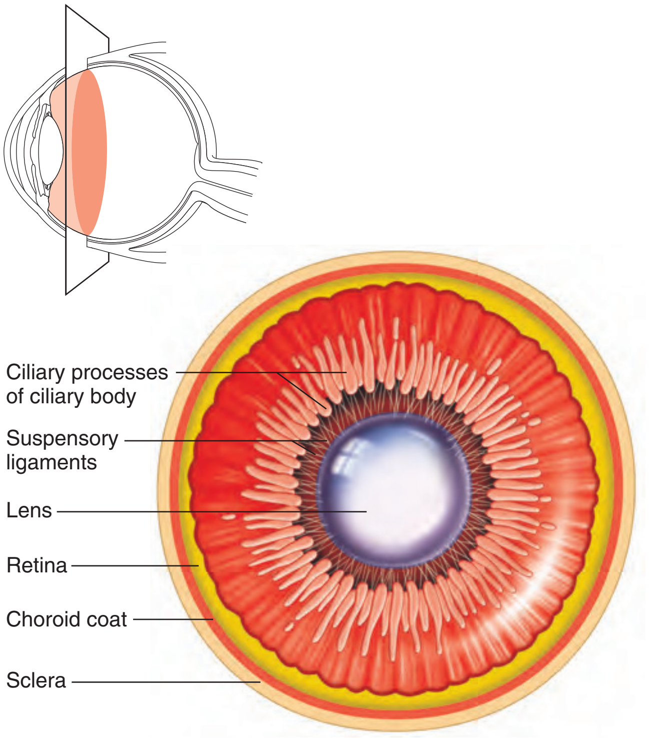


**FIGURE 10.18** Lens and ciliary body viewed from behind.

Many strong but delicate fibers, called *suspensory ligaments,* extend inward from the ciliary processes and hold the transparent **lens** in position (fig. 10.18). The distal ends of these fibers attach along the margin of a thin capsule that surrounds the lens. The body of the lens lies directly behind the iris and pupil and is composed of highly specialized epithelial cells called *lens fibers.* The cytoplasm of these cells is the transparent substance of the lens.

More than 90% of the proteins in a lens cell are lens crystallins, which aggregate into fibers. These proteins, along with the absence of organelles that scatter light (mitochondria, endoplasmic reticula, and nuclei), account for the transparency of the lens.

An eye disorder common in older people is *cataract.* The lens or its capsule slowly becomes cloudy and opaque. Cataracts are treated on an outpatient basis with surgery to remove the clouded lens and replace it with an artificial lens. Without treatment, cataracts eventually cause blindness.

The ciliary muscles and suspensory ligaments, along with the structure of the lens itself, enable the lens to adjust shape to facilitate focusing, a phenomenon called

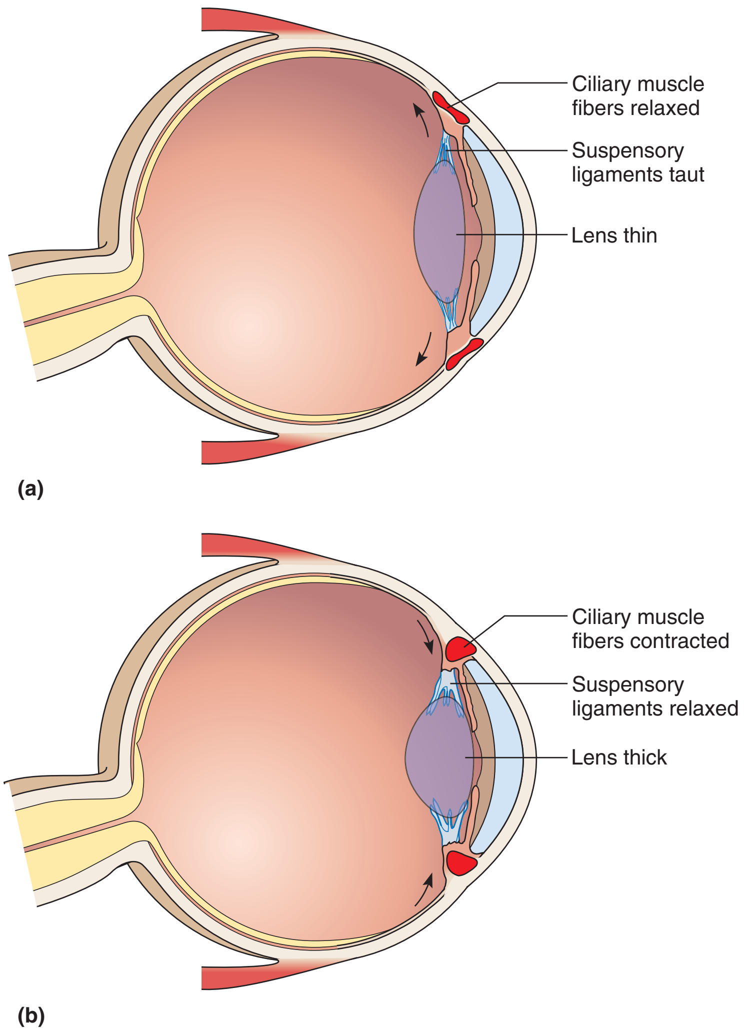

Ciliary muscle fibers relaxed
Suspensory ligaments taut
Lens thin
(a)
Ciliary muscle fibers contracted
Suspensory ligaments relaxed
Lens thick
(b)

**FIGURE 10.19** Accommodation. **(a)** The lens thins as the ciliary muscle fibers relax. **(b)** The lens thickens as the ciliary muscle fibers contract.

**accommodation** (ah-kom″o-da′shun). The lens is enclosed by a clear capsule composed largely of elastic fibers. This elastic nature keeps the lens under constant tension, and enables it to assume a globular shape. The suspensory ligaments attached to the margin of the capsule are also under tension. When they pull outward, flattening the capsule and the lens inside, the lens focuses on distant objects (fig. 10.19*a*). However, if the tension on the suspensory ligaments relaxes, the elastic lens capsule rebounds, and the lens surface becomes more convex—focused for viewing closer objects (fig. 10.19*b*).

The ciliary muscles control the actions of the suspensory ligaments in accommodation. For example, one set of these muscle fibers extends back from fixed points in the sclera to the choroid coat. When the fibers contract, the choroid coat is pulled forward, and the ciliary body shortens. This relaxes the suspensory ligaments, and the lens thickens in response (see fig. 10.19*b*). When the ciliary muscles relax, tension on the suspensory ligaments increases, and the lens becomes thinner and less convex again (see fig. 10.19*a*).

## PRACTICE

26. Describe the outer and middle layers of the eye.
27. What factors contribute to the transparency of the cornea?
28. How does the shape of the lens change during accommodation?
29. Why would reading for a long time cause eye fatigue, while looking at a distant scene is restful?

The **iris** (i′ris) is a thin diaphragm composed mostly of connective tissue and smooth muscle fibers. From the outside, the iris is the colored part of the eye. The iris extends forward from the periphery of the ciliary body and lies between the cornea and lens (see fig. 10.17). The iris divides the space (anterior cavity) separating these parts into an *anterior chamber* (between the cornea and the iris) and a *posterior chamber* containing the lens (between the iris and the vitreous body).

The epithelium on the inner surface of the ciliary body secretes a watery fluid called **aqueous humor** (a′kwe-us hu′mor) into the posterior chamber. The fluid circulates from this chamber through the **pupil** (pu′pil), a circular opening in the center of the iris, and into the anterior chamber. Aqueous humor fills the space between the cornea and lens, helps nourish these parts, and aids in maintaining the shape of the front of the eye. Aqueous humor leaves the anterior chamber through veins and a special drainage canal, the scleral venous sinus (canal of Schlemm), which is in the wall of the anterior chamber at the junction of the cornea and the sclera.

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An eye disorder called *glaucoma* develops when aqueous humor forms faster than it is removed. As fluid accumulates in the anterior chamber of the eye, fluid pressure rises and is transmitted to all parts of the eye. In time, the building pressure squeezes shut blood vessels that supply the receptor cells of the retina. Cells that are robbed of nutrients and oxygen in this way may die, and permanent blindness can result.

When diagnosed early, glaucoma can usually be treated successfully with drugs, laser surgery, or traditional surgery, all of which promote the outflow of aqueous humor. Since glaucoma in its early stages typically produces no symptoms, discovery of the condition usually depends on measuring intraocular pressure, using an instrument called a *tonometer*.

---

The smooth muscle fibers of the iris are organized into two groups, a *circular set* and a *radial set*. These muscles control the size of the pupil, through which light passes as it enters the eye. The circular set of muscle fibers acts as a sphincter. When the muscle fibers contract, the pupil gets smaller, and less light enters. Bright light stimulates the circular muscles to contract, which decreases the intensity of light entering the eye. Conversely, when the radial muscle fibers contract, the pupil's diameter increases, and more light

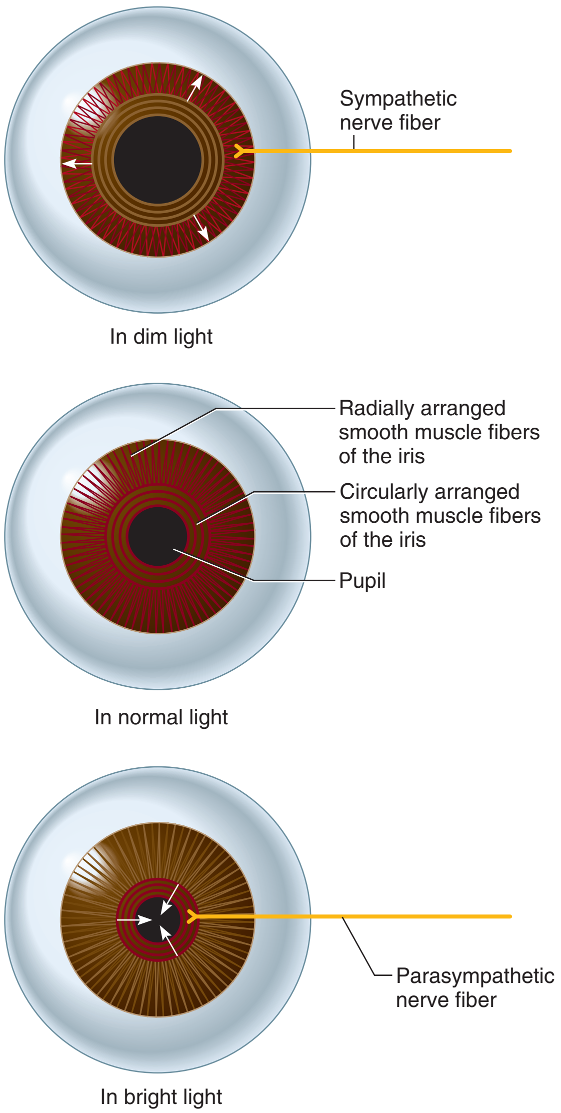
Sympathetic nerve fiber
In dim light
Radially arranged smooth muscle fibers of the iris
Circularly arranged smooth muscle fibers of the iris
Pupil
In normal light
Parasympathetic nerve fiber
In bright light

**FIGURE 10.20** Dim light stimulates the radial muscles of the iris to contract, and the pupil dilates. Bright light stimulates the circular muscles of the iris to contract, and the pupil constricts.

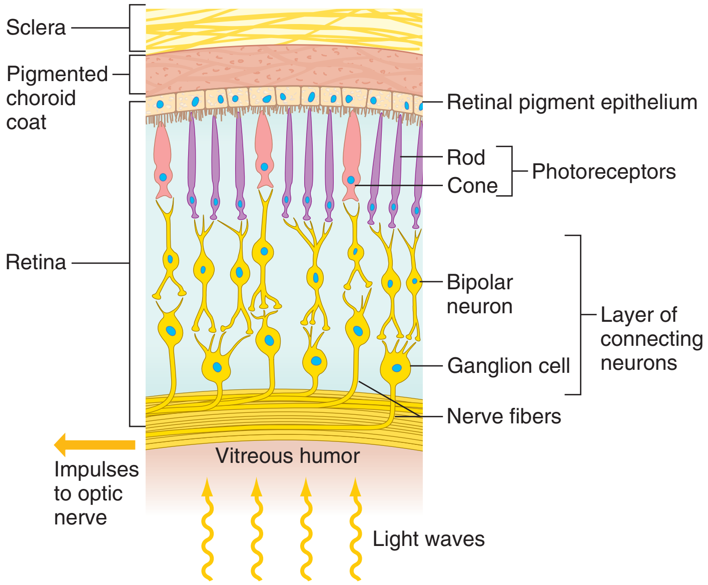
Sclera
Pigmented choroid coat
Retina
Retinal pigment epithelium
Rod
Cone
Photoreceptors
Bipolar neuron
Ganglion cell
Layer of connecting neurons
Nerve fibers
Vitreous humor
Impulses to optic nerve
Light waves

**FIGURE 10.21** The retina consists of several cell layers. Light waves penetrate a layer of connecting neurons to impinge on the rods and cones, which are the photoreceptors. The retinal pigment epithelium absorbs stray light rays.

enters (fig. 10.20). Dim light stimulates the radial muscles to contract, which dilates the pupil, allowing more light into the eye.

### *Inner Layer*

The inner layer of the wall of the eye consists of the **retina** (ret′ĭ-nah), which contains the visual receptor cells (photoreceptors). The retina is a nearly transparent sheet of tissue continuous with the optic nerve in the back of the eye and extending forward as the inner lining of the eyeball. The retina ends just behind the margin of the ciliary body.

The retina is thin and delicate, but its structure is quite complex. It has a number of distinct layers, as figures 10.21 and 10.22 illustrate.

In the central region of the retina is a yellowish spot called the *macula lutea.* A depression in its center, called the **fovea centralis** (fo′ve-ah sen-tral′is), is in the region of the retina that produces the sharpest vision (see figs. 10.17 and 10.23).

Just medial to the fovea centralis is an area called the **optic disc** (op′tik disk) (fig. 10.23). Here, nerve fibers from the retina leave the eye and join the optic nerve. A central artery and vein also pass through the optic disc. These vessels are continuous with the capillary networks of the retina, and along with vessels in the underlying choroid coat, they supply blood to the cells of the inner layer. Because the optic disc region lacks photoreceptors, it is commonly known as the *blind spot* of the eye.

The space bounded by the lens, ciliary body, and retina is the largest compartment of the eye and is called the *posterior cavity* (see fig. 10.17). It is filled with a transparent, jellylike fluid called **vitreous humor** (vit′re-us hu′mor), which along with collagen fibers forms the *vitreous body.* The vitreous body supports the internal parts of the eye and helps maintain its shape.

As a person ages, tiny, dense clumps of gel or deposits of crystal-like substances form in the vitreous humor. When these clumps cast shadows on the retina, the person sees small, moving specks in the field of vision, called *floaters.*

**PRACTICE**

30. Explain the source of aqueous humor, and trace its path through the eye.
31. How does the pupil respond to changes in light intensity?
32. Describe the structure of the retina.

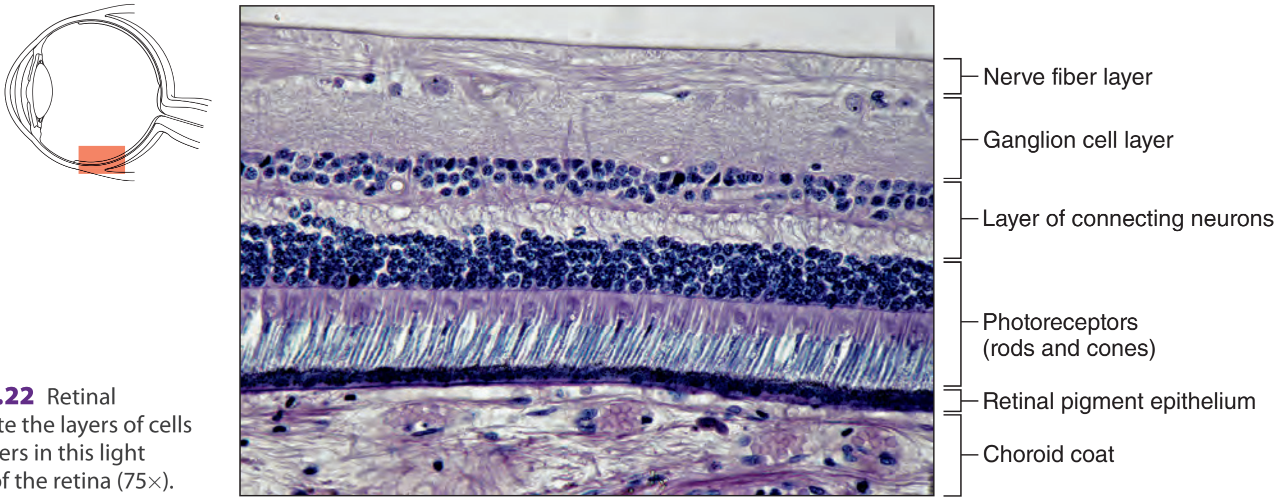
Nerve fiber layer
Ganglion cell layer
Layer of connecting neurons
Photoreceptors (rods and cones)
Retinal pigment epithelium
Choroid coat

**FIGURE 10.22** Retinal structure. Note the layers of cells and nerve fibers in this light micrograph of the retina (75×).

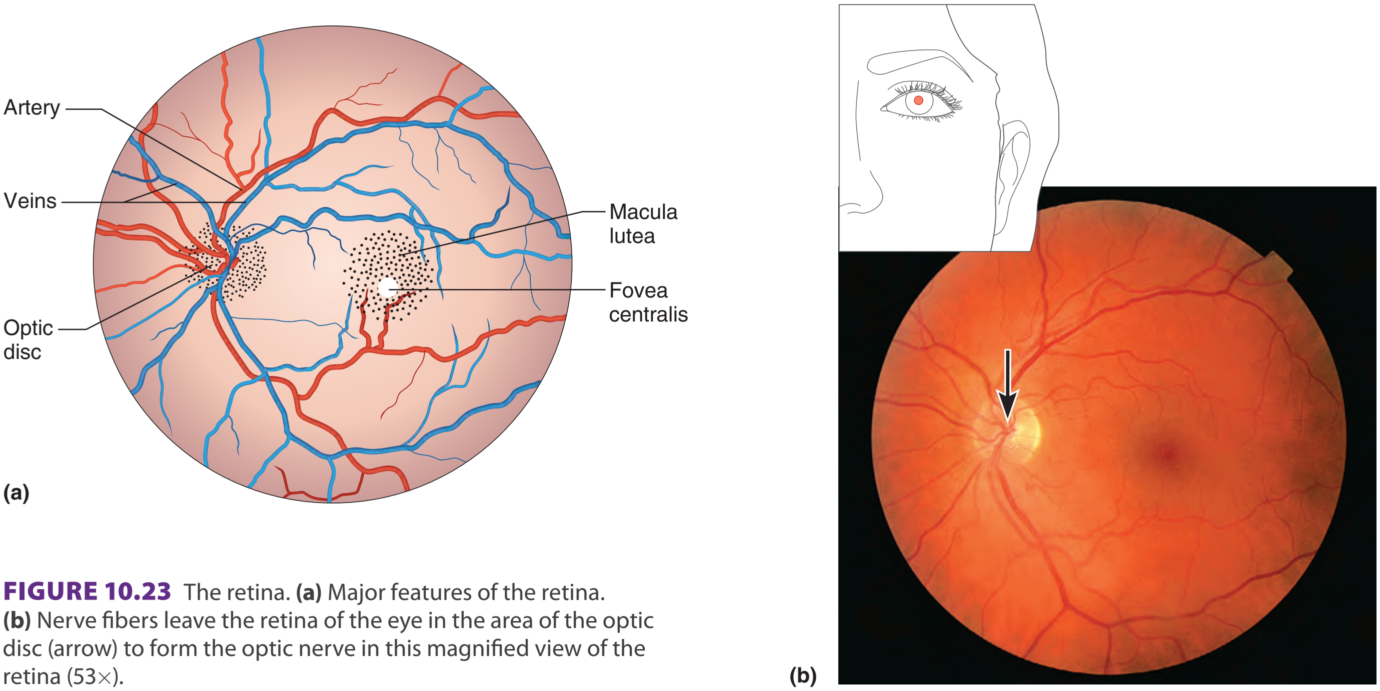
Artery
Veins
Optic disc
Macula lutea
Fovea centralis
(a)
(b)

**FIGURE 10.23** The retina. **(a)** Major features of the retina. **(b)** Nerve fibers leave the retina of the eye in the area of the optic disc (arrow) to form the optic nerve in this magnified view of the retina (53×).

## Light Refraction

When a person sees an object, either the object is giving off light, or it is reflecting light waves from another source. These light waves enter the eye, and an image of the object is focused on the retina. Focusing bends the light waves, a phenomenon called **refraction** (re-frak′shun).

Refraction occurs when light waves pass at an oblique angle from a medium of one optical density into a medium of a different optical density. This happens at the curved surface between the air and the cornea and at the curved surface of the lens itself. A lens with a *convex* surface (as in the eye) causes light waves to converge (fig. 10.24).

The convex surface of the cornea refracts light waves from outside objects. The convex surface of the lens and, to a lesser extent, the surfaces of the fluids in the chambers of the eye then refract the light again.

If eye shape is normal, light waves focus sharply on the retina, much as a motion picture image is focused on a screen for viewing. Unlike the motion picture image, however, the image that forms on the retina is upside down and reversed from left to right. The visual cortex interprets the image in its proper position.

### PRACTICE

33. What is refraction?
34. What parts of the eye provide refracting surfaces?

## Photoreceptors

Photoreceptors are modified neurons of two distinct kinds, as figure 10.21 illustrates. One group, called *rods* (rodz), have long, thin projections at their ends, and provide black

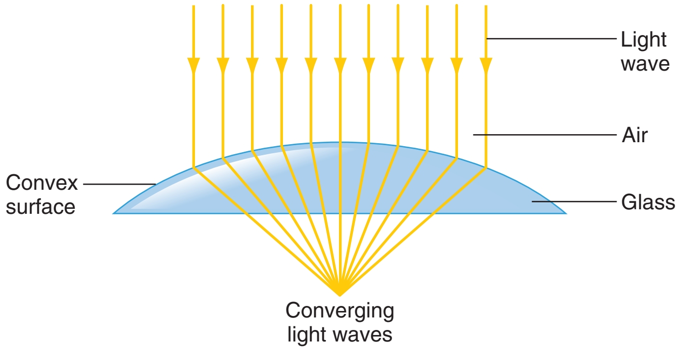

**FIGURE 10.24** A lens with a convex surface causes light waves to converge. The lens of the eye functions the same way.

and white vision. The other group, *cones* (kōnz), have short, blunt projections, and provide color vision. There is only one type of rod, but three types of cones.

Rods and cones are in a deep part of the retina, where they project into an adjacent layer of retinal pigment epithelium (RPE) that absorbs light waves the photoreceptors do not absorb. With the pigment of the choroid coat, the RPE keeps light from reflecting off surfaces inside the eye (see fig. 10.22).

Photoreceptors are stimulated only when light reaches them. A light image focused on an area of the retina stimulates some photoreceptors, and impulses travel from them to the brain. However, the impulses leaving each activated photoreceptor deliver only a fragment of the information required for the brain to interpret a complete scene.

Rods and cones contribute to different aspects of vision. Rods are hundreds of times more sensitive to light than cones and therefore can provide vision in dim light, without color. Cones detect color.

A human eye has 125 million rods and 7 million cones. A cat has three types of cone cells, but sees mostly pastels. A dog has two types of cone cells, and its visual world is much like that of a person with colorblindness. Researchers corrected colorblindness in monkeys by introducing the genes for human cone pigments into their eyes.

Rods and cones also differ in the sharpness of the perceived images, or visual acuity. Cones provide sharp images, and rods provide more general outlines of objects. Rods give less precise images because axon branches from many rods converge, so that their impulses are conducted to the brain on the same nerve fiber (fig. 10.25*a*). Thus, if a point of light stimulates a rod, the brain cannot tell which one of many receptors has been stimulated. Convergence of impulses is less common among cones. When a cone is stimulated, the brain can pinpoint the stimulation more accurately (fig. 10.25*b*).

The fovea centralis, the area of sharpest vision, lacks rods but contains densely packed cones with few or no converging fibers (see fig. 10.17). Also in the fovea centralis, the overlying layers of the retina and the retinal blood vessels are displaced to the sides, more fully exposing photoreceptors to incoming light. Consequently, to view something in detail, a person moves the eyes so that the important part of an image falls on the fovea centralis.

## Photopigments

Both rods and cones contain light-sensitive pigments that decompose when they absorb light energy. The light-sensitive biochemical in rods is called **rhodopsin** (ro-dop′sin), or *visual purple*. In the presence of light, rhodopsin molecules are broken down into a colorless protein called *opsin* and a yellowish substance called *retinal* (retinene) that is synthesized from vitamin A.

Decomposition of rhodopsin molecules activates an enzyme that initiates a series of reactions altering the permeability of the rod cell membrane. As a result, a complex pattern of nervous stimulation originates in the retina. The impulses are conducted away from the retina along the optic nerve into the brain, where they are interpreted as vision.

In bright light, nearly all of the rhodopsin in the rods of the retina decomposes, greatly reducing rod sensitivity. In dim light, however, regeneration of rhodopsin from opsin and retinal is faster than rhodopsin breakdown. ATP provides the energy required for this regeneration (see chapter 4, p. 91).

Poor vision in dim light, called nightblindness, results from vitamin A deficiency. Lack of the vitamin reduces the supply of retinal, rhodopsin production falls, and rod sensitivity is low. Supplementing the diet with vitamin A is used to treat nightblindness.

In one form of the inherited condition, Leber congenital amaurosis, absence of an enzyme in the RPE prevents production of retinal from vitamin A, causing nightblindness that progresses to full blindness by early adulthood. Gene therapy that introduces functional copies of the mutant gene into the RPE has enabled more than 200 people receiving the experimental treatment to see.

The light-sensitive pigments in cones, as in the rods, are composed of retinal and protein. In cones, however, three types of opsin proteins, different from the protein portion of rhodopsin found in rods, combine with retinal to form the three cone pigments. The three types of cones each contain one of these three photopigments.

The wavelength of light determines the color that the brain perceives from it. For example, the shortest wavelengths of visible light are perceived as violet, and the longest are perceived as red. One type of cone pigment (erythrolabe) is most sensitive to red light waves, another (chlorolabe) to green light waves, and the third (cyanolabe) to blue light waves. The color a person perceives depends on which set of cones or combination of sets the light in a given image stimulates. If all three sets of cones are stimulated, the person senses the light as white, and if none are stimulated, the person senses

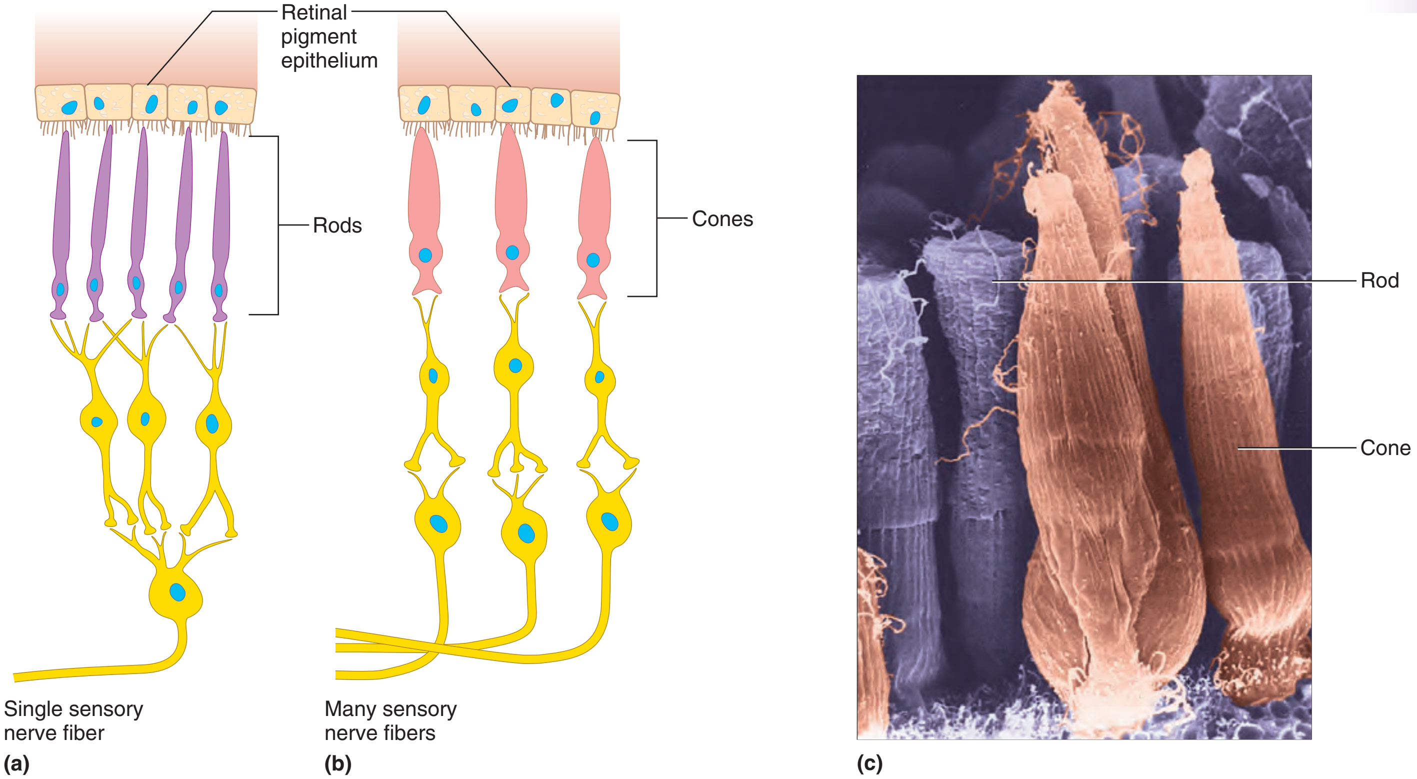
Retinal pigment epithelium
Rods
Cones
Single sensory nerve fiber
(a)
Many sensory nerve fibers
(b)
Rod
Cone
(c)

**FIGURE 10.25** Rods and cones are photoreceptors. **(a)** A single sensory nerve fiber transmits impulses from several rods to the brain. **(b)** Separate sensory nerve fibers transmit impulses from cones to the brain. **(c)** Scanning electron micrograph of rods and cones (1,350×).

black. Different forms of colorblindness result from lack of different types of cone pigments.

## Visual Pathways

Visual pathways conduct impulses from the retina to the visual cortex, where they are perceived as vision. The pathways begin as the axons of the retinal neurons leave the eyes to form the *optic nerves* (fig. 10.26). Just anterior to the pituitary gland, these nerves give rise to the X-shaped *optic chiasma* (op′tik ki-az′mah), and within the chiasma, some of the fibers cross over. More specifically, the fibers from the nasal (medial) half of each retina cross over, but those from the temporal (lateral) sides do not. Thus, fibers from the nasal half of the left eye and the temporal half of the right eye form the *right optic tract,* and fibers from the nasal half of the right eye and the temporal half of the left eye form the *left optic tract.*

Just before the nerve fibers reach the thalamus, a few of them enter nuclei that function in various visual reflexes. Most of the fibers, however, enter the thalamus and synapse in its posterior portion (lateral geniculate body). From this region, the visual impulses enter nerve pathways called *optic radiations,* which lead to the visual cortex of the occipital lobes.

**PRACTICE**

35. Distinguish between the rods and cones of the retina.
36. Explain the roles of visual pigments.
37. Trace an impulse from the retina to the visual cortex.

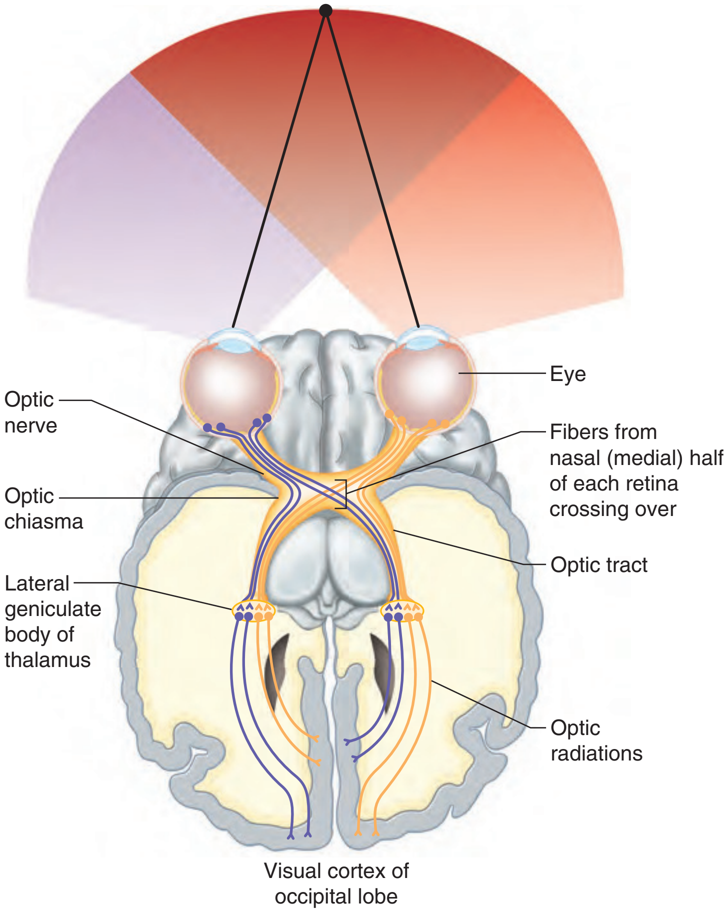
Eye
Optic nerve
Fibers from nasal (medial) half of each retina crossing over
Optic chiasma
Optic tract
Lateral geniculate body of thalamus
Optic radiations
Visual cortex of occipital lobe

**FIGURE 10.26** APR A visual pathway includes the optic nerve, optic chiasma, optic tract, and optic radiations.

# Summary Outline

### 10.1 Introduction (p. 274)

*Sensory receptors sense changes in their surroundings.*

### 10.2 Receptors, Sensations, and Perception (p. 274)

1. Types of receptors
   a. Each type of receptor is most sensitive to a distinct type of stimulus.
   b. The major types of receptors are chemoreceptors, pain receptors, thermoreceptors, mechanoreceptors, and photoreceptors.
2. Sensations
   a. A sensation is the awareness of sensory stimulation.
   b. A particular part of the cerebral cortex interprets every impulse reaching it in a specific way.
   c. The cerebral cortex projects a sensation back to the region of stimulation.
3. Sensory adaptation may involve receptors becoming unresponsive or inhibition along the CNS pathways leading to the sensory regions of the cerebral cortex.

### 10.3 General Senses (p. 275)

*General senses are associated with receptors in the skin, muscles, joints, and viscera.*

1. Touch and pressure senses
   a. Free ends of sensory nerve fibers are receptors for the sensation of itching.
   b. Tactile corpuscles are receptors for the sensation of light touch.
   c. Lamellated corpuscles are receptors for the sensation of heavy pressure.
2. Temperature senses
   Temperature receptors include two sets of free nerve endings that are warm and cold receptors.
3. Sense of pain
   a. Pain receptors are free nerve endings that tissue damage stimulates.
   b. Visceral pain
      (1) Pain receptors are the only receptors in viscera that provide sensations.
      (2) Pain sensations produced from visceral receptors may feel as if they are coming from some other body part, called referred pain.
      (3) Visceral pain may be referred because sensory impulses from the skin and viscera travel on common nerve pathways.
   c. Pain nerve fibers
      (1) The two main types of pain fibers are acute pain fibers and chronic pain fibers.
      (2) Acute pain fibers conduct impulses rapidly. Chronic pain fibers conduct impulses more slowly.
      (3) Pain impulses are processed in the gray matter of the spinal cord and ascend to the brain.
      (4) Within the brain, pain impulses pass through the reticular formation before being conducted to the cerebral cortex.
   d. Regulation of pain impulses
      (1) Awareness of pain occurs when pain impulses reach the thalamus.
      (2) The cerebral cortex determines pain intensity and locates its source.
      (3) Impulses descending from the brain stimulate neurons to release pain-relieving neuropeptides, such as enkephalins.

### 10.4 Special Senses (p. 278)

*Special senses have receptors within large, complex sensory organs of the head.*

### 10.5 Sense of Smell (p. 278)

1. Olfactory receptors
   a. Olfactory receptors are chemoreceptors that are stimulated by chemicals dissolved in liquid.
   b. Olfactory receptors function with taste receptors and aid in food selection.
2. Olfactory organs
   a. Olfactory organs consist of receptors and supporting cells in the nasal cavity.
   b. Olfactory receptor cells are bipolar neurons with cilia.
3. Olfactory pathways
   Impulses travel from the olfactory receptor cells through the olfactory nerves, olfactory bulbs, and olfactory tracts to interpreting centers in the temporal and frontal lobes of the cerebrum.
4. Olfactory stimulation
   a. Olfactory impulses may result when odorant molecules bind cell surface olfactory receptors on cilia of receptor cells. The binding pattern encodes a specific odor, which is interpreted in the brain.
   b. The sense of smell adapts rapidly.

### 10.6 Sense of Taste (p. 280)

1. Taste receptors
   a. Taste buds consist of taste (receptor) cells and supporting cells.
   b. Taste cells have taste hairs.
   c. Taste hair surfaces have receptors to which chemicals bind, stimulating impulses.
2. Taste sensations
   a. The five primary taste sensations are sweet, sour, salty, bitter, and umami.
   b. Various taste sensations result from the stimulation of one or more types of taste receptors.
   c. A single taste receptor cell detects only one of the five tastes, but receptors corresponding to different tastes are scattered on the tongue.
3. Taste pathways
   a. Sensory impulses from taste receptors travel on fibers of the facial, glossopharyngeal, and vagus nerves.
   b. These impulses are conducted to the medulla oblongata and then ascend to the thalamus, from which they are conducted to the gustatory cortex in the parietal lobes.

### 10.7 Sense of Hearing (p. 282)

1. Outer ear
   The outer ear collects sound waves of vibrating objects.
2. Middle ear
   Auditory ossicles of the middle ear conduct sound waves from the eardrum to the oval window of the inner ear.
3. Auditory tube
   The auditory tube connects the middle ear to the nasopharynx and helps maintain equal air pressure on both sides of the eardrum.
4. Inner ear
   a. The inner ear is a complex system of connected tubes and chambers—the osseous and membranous labyrinths.
   b. The spiral organ contains hearing receptors that are stimulated by vibrations in the fluids of the inner ear.
   c. Different frequencies of vibrations stimulate different sets of receptor cells.

5. Auditory pathways
   a. Auditory nerve fibers conduct impulses to the auditory cortices of the temporal lobes.
   b. Some auditory nerve fibers cross over, so that impulses arising from each ear are interpreted on both sides of the brain.

**10.8 Sense of Equilibrium (p. 286)**

1. Static equilibrium
   Static equilibrium maintains the stability of the head and body when they are motionless.
2. Dynamic equilibrium
   a. Dynamic equilibrium balances the head and body when they are moved or rotated suddenly.
   b. Other structures that help maintain equilibrium include the eyes and mechanoreceptors associated with certain joints.

**10.9 Sense of Sight (p. 289)**

1. Visual accessory organs
   Visual accessory organs include the eyelids, lacrimal apparatus, and extrinsic muscles of the eyes.
2. Structure of the eye
   a. The wall of the eye has an outer (fibrous), a middle (vascular), and an inner (nervous) layer.
      (1) The outer layer is protective, and its transparent anterior portion (cornea) refracts light entering the eye.
      (2) The middle layer is vascular and contains melanin that keeps the inside of the eye dark.
      (3) The inner layer contains the photoreceptors.
   b. The lens is a transparent, elastic structure. Ciliary muscles control its shape.
   c. The lens must thicken to focus on close objects.
   d. The iris is a muscular diaphragm that controls the amount of light entering the eye.
   e. Spaces within the eye are filled with fluids that help maintain its shape.
3. Light refraction
   The cornea and lens refract light waves to focus an image on the retina.
4. Photoreceptors
   a. Photoreceptors are rods and cones.
   b. Rods are responsible for colorless vision in dim light, and cones provide color vision.
5. Photopigments
   a. A light-sensitive pigment in rods decomposes in the presence of light and triggers a complex series of reactions that initiate impulses.
   b. Color vision comes from three sets of cones containing different light-sensitive pigments.
6. Visual pathways
   a. Nerve fibers from the retina form the optic nerves.
   b. Some fibers cross over in the optic chiasma.
   c. Most of the fibers enter the thalamus and synapse with others that continue to the visual cortex in the occipital lobes.

## CHAPTER ASSESSMENTS

**10.1 Introduction**

**1.** Distinguish between general senses and special senses. (p. 274)

**10.2 Receptors, Sensations, and Perception**

**2.** Match each sensory receptor to the type of stimulus to which it is likely to respond. (p. 274)

(1) chemoreceptor
(2) pain receptor
(3) thermoreceptor
(4) mechanoreceptor
(5) photoreceptor

A. approaching headlights
B. a change in blood pressure
C. the smell of roses
D. an infected tooth
E. a cool breeze

**3.** Explain the difference between a sensation and a perception. (p. 274)

**4.** Explain the projection of a sensation. (p. 274)

**5.** You fill up the tub to take a hot bath, but the water is too hot to the touch. You try a second and third time, and within a few seconds it feels fine. Which of the following is the most likely explanation? (p. 274)

a. The water has cooled down unusually quickly.
b. Your ability to sense heat has adapted.
c. Your nervous system is suddenly not functioning properly.
d. Your ability to sense cold has adapted.

**10.3 General Senses**

**6.** Describe the functions of free nerve endings, tactile corpuscles, and lamellated corpuscles. (p. 275)

**7.** Explain why pain may be referred, and provide an example. (p. 276)

**10.4 Special Senses**

**8.** Identify the location of the receptors for smell, taste, hearing, equilibrium, and sight. (p. 278)

**10.5 Sense of Smell**

**9.** Which two of the following are part of the olfactory organs? (p. 279)

a. olfactory receptor cells
b. columnar epithelial cells in the nasal mucosa
c. the brain
d. the eyes

**10.** Trace an impulse from the olfactory receptor cells to the interpreting center of the cerebrum. (p. 280)

**10.6 Sense of Taste**

**11.** Salivary glands are important in taste because ____________ . (p. 281)

a. they provide the fluid in which food molecules dissolve
b. the taste receptors are located in salivary glands
c. salivary glands are part of the brain
d. they produce enzymes to break down the food

**12.** Name the five primary taste sensations. (p. 281)

**13.** Trace the pathway of an impulse from a taste receptor to the interpreting center of the cerebrum. (pp. 281–282)

**10.7 Sense of Hearing**

**14.** Match the ear area with the associated structure. (p. 282)

(1) outer ear
(2) middle ear
(3) inner ear

A. cochlea
B. eardrum
C. auditory ossicles

**15.** Trace the path of sound waves from the external acoustic meatus to the hearing receptors. (p. 282)

**16.** Describe the functions of the auditory ossicles. (p. 283)

**17.** The function of the auditory tube is to ___________ . (p. 283)

a. equalize air pressure on both sides of the eardrum
b. transmit sound vibrations to the eardrum
c. contain the hearing receptors
d. connect the ears

**18.** Distinguish between the osseous and membranous labyrinths. (p. 283)

**19.** Describe the cochlea and its function. (p. 283)

**20.** Trace an impulse from the spiral organ to the interpreting centers of the cerebrum. (pp. 283–285)

**21.** Which of the following best describes hearing receptor "hair cells"? (p. 284)

a. They are neurons.
b. They lack ion channels.
c. They are epithelial, but function like neurons.
d. They are built of the protein keratin.

**22.** Explain how a hearing receptor stimulates a sensory neuron. (p. 284)

### 10.8 Sense of Equilibrium

**23.** Contrast static equilibrium and dynamic equilibrium. (p. 286)

**24.** Describe the organs of static and dynamic equilibrium and their functions. (p. 286)

### 10.9 Sense of Sight

**25.** Match the visual accessory organ with its function. (p. 289)

(1) eyelid
(2) conjunctiva
(3) lacrimal gland
(4) extrinsic muscles

A. move the eye
B. covers the eye
C. lines the eyelids
D. produces tears

**26.** Name the three layers of the eye wall and describe the functions of each layer. (p. 290)

**27.** Explain why looking at a close object causes fatigue, in terms of how accommodation is accomplished. (p. 293)

**28.** Explain the mechanisms of pupil constriction and pupil dilation. (p. 293)

**29.** All of the following are compartments within the eye. In which one is vitreous humor found? (p. 294)

a. anterior chamber
b. posterior chamber
c. anterior cavity
d. posterior cavity

**30.** Distinguish between the fovea centralis and the optic disc. (p. 294)

**31.** Explain how light is focused on the retina. (p. 295)

**32.** Distinguish between rods and cones. (p. 296)

**33.** Explain why cone vision is generally more acute than rod vision. (p. 296)

**34.** Describe the function of rhodopsin (p. 296)

**35.** Explain why rod vision may be more important under dim light conditions. (p. 296)

**36.** Describe the relationship between light wavelength and color vision. (p. 297)

**37.** Trace an impulse from the retina to the visual cortex. (p. 297)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 6.2, 9.14, 10.2, 10.9

**1.** PET (positron emission tomography) scans of the brains of people who have been blind since birth reveal high neural activity in the visual centers of the cerebral cortex when these people read Braille. However, when sighted individuals run their fingers over the raised letters of Braille, the visual centers do not show increased activity. Explain these experimental results.

### OUTCOMES 10.2, 10.5

**2.** Loss of the sense of smell often precedes the major symptoms of Alzheimer disease and Parkinson disease. What additional information is needed to use this association to prevent or treat these diseases?

### OUTCOMES 10.5, 10.6

**3.** Describe how the taste of a medicine might be modified from sour to sweet, so that children would be more willing to take it.

### OUTCOMES 10.2, 10.7, 10.8

**4.** People who are deaf due to cochlear damage may still suffer from motion sickness. Why?

### OUTCOMES 10.2, 10.8

**5.** Labyrinthitis is an inflammation of the inner ear. What symptoms would you expect in a patient with this disorder?

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# 11

# Endocrine System

*The endocrine system produces hormones, which act within an individual. Humans may also produce pheromones, which affect other individuals and may play a role in mate selection, as they do in rodents and insects.*

Smelly T-shirts. The endocrine system produces hormones, which are biochemicals that send messages within an individual. Less well understood are pheromones, which are chemical signals sent between individuals of a species. In insects and rodents, pheromones stimulate mating behavior. Experiments suggest that this may be the case with humans, too.

Mice and rats choose mates that are dissimilar to themselves with respect to a group of genes that provide immunity. Their sense of smell helps them discern appropriate mates. Biologists hypothesize that choosing mates based on scent may protect offspring in two ways—it prevents close relatives from mating, and it may team immune systems with different types of strengths.

Researchers have traced mouse social and mating behavior to receptors in the olfactory epithelium, in the nasal cavity. The receptors—called trace-amine-associated receptors—are attuned to molecules in mouse urine that direct social behavior. The genes that encode the receptors are also in the human genome.

To test whether heterosexual humans use the sense of smell to respond to pheromones in mate selection as rodents do, researchers in Switzerland recruited forty-nine young women and forty-four young men. Each participant donated DNA, which was typed for human versions of genes that affect mating in rodents. The women used nasal spray for two weeks to clear their nasal passages. The men wore the same T-shirt on two consecutive days, using no deodorant or soap and avoiding contact with anything smelly that could linger. Each woman was then given three T-shirts from men genetically similar to her and three T-shirts from men genetically dissimilar to her, not knowing which shirts came from which men.

The women rated the shirts on intensity, pleasantness, and sexiness. Like the mice and rats, women preferred the sweaty T-shirts from the men least like them genetically.

Another, more specific experiment supported these findings. Women were given vials of fluid to sniff that either contained or did not contain a component of male sweat called androstadienone. Although they didn't know which samples they were sniffing, the women consistently reported mood elevation and sexual arousal when they smelled the androstadienone. In addition, their saliva had increased amounts of cortisol, a hormone that raises the blood sugar level, when they smelled the chemical, suggesting that it might be a human pheromone. Despite the mounting scientific evidence for human pheromones, a definitive human pheromone has not yet been described.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 11.1 Introduction

1. Describe the secretions of the endocrine system. (p. 302)
2. Distinguish between paracrine and autocrine secretions. (p. 302)
3. Distinguish between endocrine and exocrine glands. (p. 302)

### 11.2 General Characteristics of the Endocrine System

4. Explain how the nervous and endocrine systems are alike and how they are different. (p. 302)
5. Describe the source of specificity of the endocrine system. (p. 302)
6. Name some functions of hormones. (p. 302)

Anatomy & Physiology REVEALED aprevealed.com **Module 8** Endocrine System

**11.3 Hormone Action**

**7.** Explain how steroid and nonsteroid hormones affect target cells. (p. 304)

**11.4 Control of Hormonal Secretions**

**8.** Discuss how negative feedback mechanisms regulate hormonal secretions. (p. 306)

**9.** Explain how the nervous system controls secretion of hormones. (p. 307)

**11.5–11.10 Pituitary Gland–Other Endocrine Glands**

**10.** Name and describe the locations of the major endocrine glands, and list the hormones they secrete. (pp. 307–319)

**11.** Describe the functions of the hormones that endocrine glands secrete. (pp. 307–321)

**12.** Explain how the secretion of each hormone is regulated. (pp. 307–321)

**11.11 Stress and Health**

**13.** Describe how the body responds to stress. (p. 321)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**-crin** [to secrete] endo*crine*: Pertaining to internal secretions.

**diuret-** [to pass urine] *diuret*ic: Substance that promotes urine production.

**endo-** [within] *endo*crine gland: Gland that releases its secretion internally into a body fluid.

**exo-** [outside] *exo*crine gland: Gland that releases its secretion to the outside through a duct.

**hyper-** [above] *hyper*thyroidism: Condition resulting from an above-normal secretion of thyroid hormone.

**hypo-** [below] *hypo*thyroidism: Condition resulting from a below-normal secretion of thyroid hormone.

**para-** [beside] *para*thyroid glands: Set of glands on the posterior surface of the thyroid gland.

**toc-** [birth] oxy*toc*in: Hormone that stimulates the uterine muscles to contract during childbirth.

**-tropic** [influencing] adrenocortico*tropic* hormone: Hormone that influences secretions from the adrenal cortex.

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## 11.1 Introduction

Regulating the functions of the human body to maintain homeostasis is an enormous job. Two organ systems function in coordination to enable body parts to communicate with each other and to adjust constantly to changing incoming signals. The nervous system is one biological communication system. The other is the endocrine system.

The **endocrine system** includes cells, tissues, and organs, collectively called endocrine glands, that secrete substances called **hormones** (hor′mōnz) into the internal environment. The hormones diffuse from the interstitial fluid into the bloodstream, and eventually act on cells called **target cells** some distance away.

Some glands secrete substances into the interstitial fluid, but because these secretions are rapidly broken down, they do not reach the bloodstream and are not hormones by the traditional definition. However, they do function similarly as messenger molecules and are sometimes referred to as "local hormones." These include **paracrine** secretions, which affect only neighboring cells, and **autocrine** secretions, which affect only the secreting cell itself.

A different group of glands, called exocrine glands, secrete outside the internal environment. Sweat, secreted by sweat glands and reaching the surface of the skin, is one example of an exocrine secretion (see chapter 6, p. 134).

### PRACTICE

1. What are the components of the endocrine system?
2. How do paracrine and autocrine secretions function differently than traditionally defined hormones?
3. Distinguish between endocrine and exocrine glands.

## 11.2 General Characteristics of the Endocrine System

Both the endocrine system and the nervous system oversee cell-to-cell communication using chemical signals that bind to receptor molecules. Table 11.1 summarizes some similarities and differences between the nervous and endocrine systems. In contrast to the nervous system, in which neurons release neurotransmitter molecules into synapses, the cells of the endocrine system release hormones into the bloodstream, which carries these messenger molecules everywhere (fig. 11.1). However, the endocrine system is no less precise, because only target cells can respond to a hormone. A hormone's target cells have specific receptors that other cells do not have. These receptors are proteins or glycoproteins with binding sites for a specific hormone.

Endocrine glands and their hormones help regulate metabolic processes. They control the rates of certain chemical reactions, aid in the transport of substances across cell membranes, and help regulate water and electrolyte balances. They also play vital roles in reproduction, development, and growth.

**TABLE 11.1 A Comparison Between the Nervous System and the Endocrine System**

| | Nervous System | Endocrine System |
|---|---|---|
| **Cells** | Neurons | Epithelial and others |
| **Chemical signal** | Neurotransmitter | Hormone |
| **Specificity of response** | Receptors on postsynaptic cell | Receptors on target cell |
| **Speed of onset** | Seconds | Seconds to hours |
| **Duration of action** | Very brief unless neuronal activity continues | May be brief or may last for days even if secretion ceases |

Specialized cells in the liver, heart, and gastrointestinal tract produce some hormones. However, the major endocrine glands are the pituitary gland, thyroid gland, parathyroid glands, adrenal glands, pancreas, pineal gland, reproductive glands (testes and ovaries), kidneys, and thymus (fig. 11.2).

## PRACTICE

4. Explain how the nervous and endocrine systems are alike and how they differ.
5. What determines whether a cell is a target cell for a particular hormone?
6. State some functions of hormones.

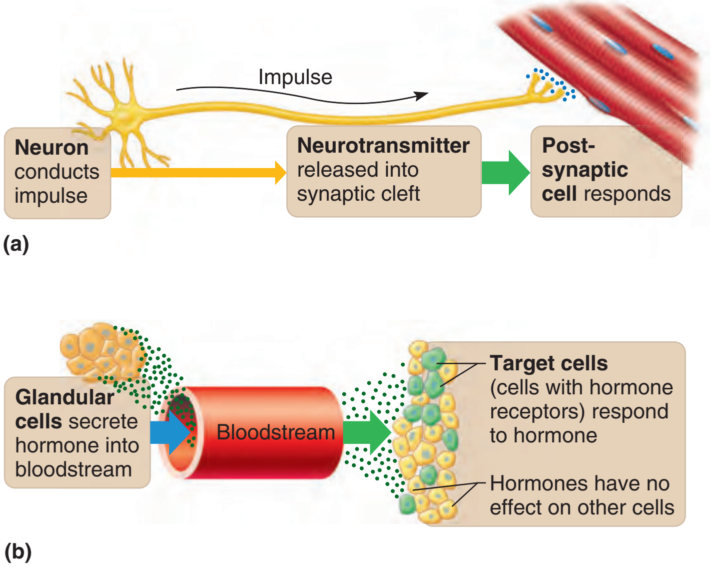

Impulse
Neuron conducts impulse
Neurotransmitter released into synaptic cleft
Post-synaptic cell responds
(a)
Glandular cells secrete hormone into bloodstream
Bloodstream
Target cells (cells with hormone receptors) respond to hormone
Hormones have no effect on other cells
(b)

**FIGURE 11.1** Chemical communication takes place in the nervous system and the endocrine system. In both cases, cells respond to chemicals released from other cells. **(a)** Neurons release neurotransmitters into a synapse, affecting postsynaptic cells. **(b)** Glands release hormones into the bloodstream. Blood carries hormone molecules throughout the body, but only target cells respond.

Q *What do postsynaptic cells and target cells have in common that allow them to respond to secreted chemicals?*

**Answers can be found in Appendix F on page 582.**

## 11.3 | Hormone Action

Most hormones are of two general types. They are either steroids (or steroidlike substances) synthesized from cholesterol, or they are amines, peptides, polypeptides and proteins, or glycoproteins synthesized from amino acids (table 11.2). Hormones can stimulate changes in target cells even in extremely low concentrations.

### Steroid Hormones

Steroid molecules consist of complex rings of carbon and hydrogen atoms, and some oxygen atoms (see fig. 2.16, p. 52). Steroids differ according to the types and numbers of atoms attached to these rings and the ways they are joined.

Steroid hormones are insoluble in water. They are carried in the bloodstream weakly bound to plasma

### CAREER CORNER

### Licensed Practical Nurse

The man has been suffering from cancer for many months and now is bedridden. He receives hospice care in his home. Three times a week, a licensed practical nurse (LPN) arrives to take the man's vital signs, check that he is receiving the proper doses of medications to stay comfortable, and help the family by answering their questions about caring for their loved one. The LPN might suggest or demonstrate ways to bathe or feed the patient, and change the bedding. Should the patient exhibit signs of active dying or require further medication, or if a change in status has occurred, the LPN reports the information to the registered nurse or physician assigned to the case.

An LPN is an entry-level nursing position. In the United States, becoming an LPN requires completing a post–high school program that typically takes one year. In some states an LPN is called a licensed vocational nurse, or LVN. An LPN must pass a national licensure exam. LPNs work in hospitals, nursing homes, assisted living facilities, physicians' offices, and with home health-care agencies.

**TABLE 11.2** Types of Hormones

| Type of Compound | Formed From | Examples |
|---|---|---|
| Steroids | Cholesterol | Estrogen, testosterone, aldosterone, cortisol |
| Amines | Amino acids | Norepinephrine, epinephrine , thyroid hormones |
| Peptides | Amino acids | Antidiuretic hormone, oxytocin, thyrotropin-releasing hormone |
| Polypeptides and proteins | Amino acids | Parathyroid hormone, growth hormone, prolactin |
| Glycoproteins | Protein and carbohydrate | Follicle-stimulating hormone, luteinizing hormone, thyroid-stimulating hormone |

proteins in a way that allows them to be released in sufficient quantity in the vicinity of their target cells. However, unlike amine, peptide, and protein hormones, steroid hormones are soluble in lipids.

Steroid hormones can diffuse into cells relatively easily, because lipids make up the bulk of cell membranes and steroid molecules are lipid-soluble. Steroid hormones may enter any cell in the body, but only target cells will respond. When a steroid hormone molecule enters a target cell, the following events occur (fig. 11.3):

1. The lipid-soluble steroid hormone diffuses through the cell membrane.
2. The steroid hormone binds a specific protein molecule—the receptor for that hormone.
3. The resulting hormone-receptor complex binds in the nucleus to specific sequences of the target cell's DNA, activating transcription of specific genes into messenger RNA (mRNA) molecules.
4. The mRNA molecules leave the nucleus and enter the cytoplasm.
5. Translation of mRNA molecules leads to the synthesis of specific proteins.

The newly synthesized proteins, which may be enzymes, transport proteins, or even hormone receptors, carry out the specific effects associated with the particular steroid hormone.

## Nonsteroid Hormones

Nonsteroid hormones, such as amines, peptides, and proteins, usually bind receptors in target cell membranes. Each of these receptor molecules is a protein with a *binding site* and an *activity site.* A hormone molecule delivers its message to its target cell by uniting with the binding site of its receptor. This combination stimulates the receptor's activity site to interact with other membrane proteins. The hormone that triggers this cascade of biochemical activity is called a *first messenger.* The biochemicals in the cell that induce changes in response to the hormone's binding are called *second messengers.* The entire process of chemical communication, from outside cells to inside, is called **signal transduction.**

The second messenger associated with one group of hormones is *cyclic adenosine monophosphate,* also called **cyclic AMP (cAMP)** (sī′klik ay em pee). This mechanism works as follows (fig. 11.4):

1. A hormone binds to its receptor.
2. The resulting hormone-receptor complex activates a membrane protein called a *G protein.*
3. The G protein activates an enzyme called *adenylate cyclase,* which is a membrane protein.
4. In the cytoplasm, activated adenylate cyclase catalyzes the formation of cAMP from ATP.
5. cAMP activates another set of enzymes, called protein kinases, which transfer phosphate groups from ATP to their substrate molecules, which are specific proteins in the cell. This action, called phosphorylation, alters the shapes of these substrate molecules, thereby activating them.

The activated proteins then alter various cellular processes, bringing about the characteristic effect of the hormone.

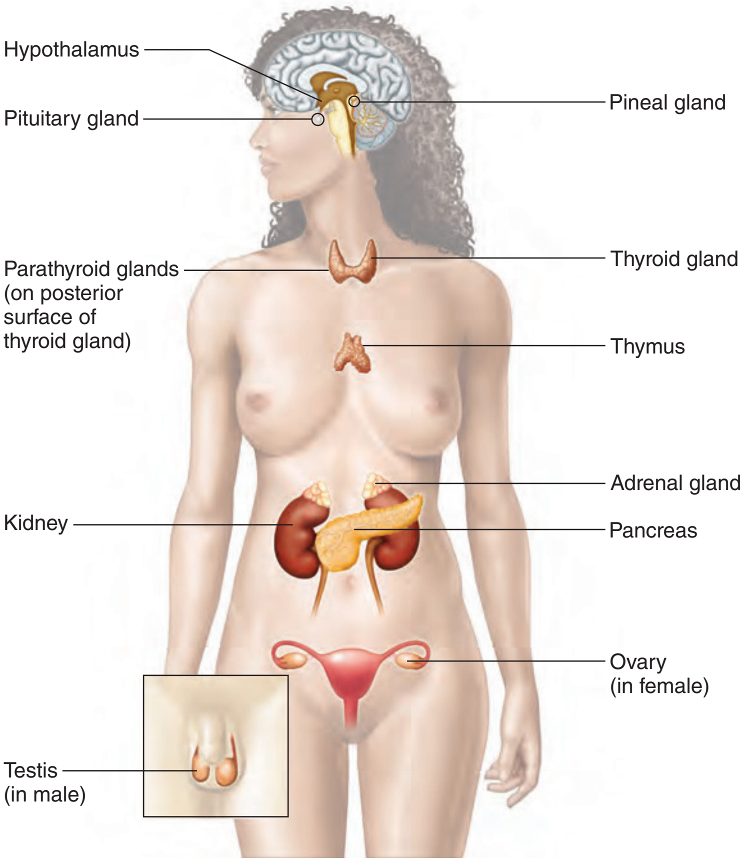


**FIGURE 11.2** Locations of the major endocrine glands. The pituitary, thyroid, parathyroid, adrenal glands, and the pancreas are the main topics of this chapter. The functions of the other glands are described in more detail in subsequent chapters.

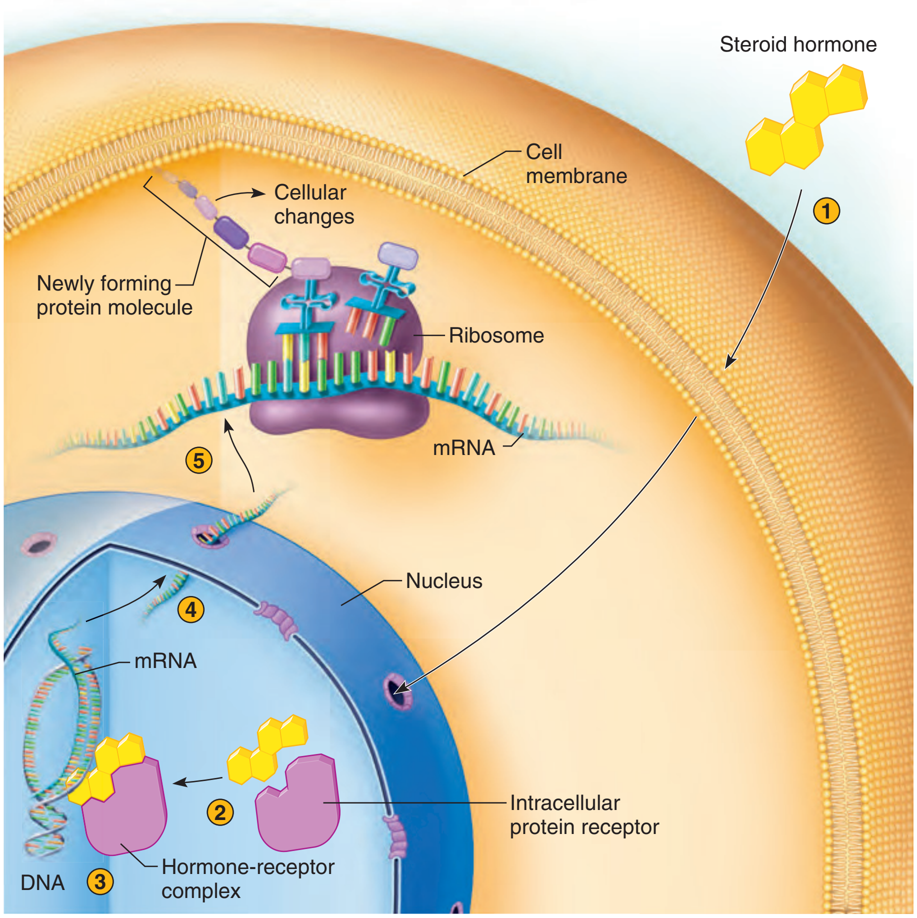

Steroid hormone
①
Cell membrane
Cellular changes
Newly forming protein molecule
Ribosome
mRNA
⑤
④
Nucleus
mRNA
②
Intracellular protein receptor
DNA
③
Hormone-receptor complex

**FIGURE 11.3** APR Steroid hormone action.

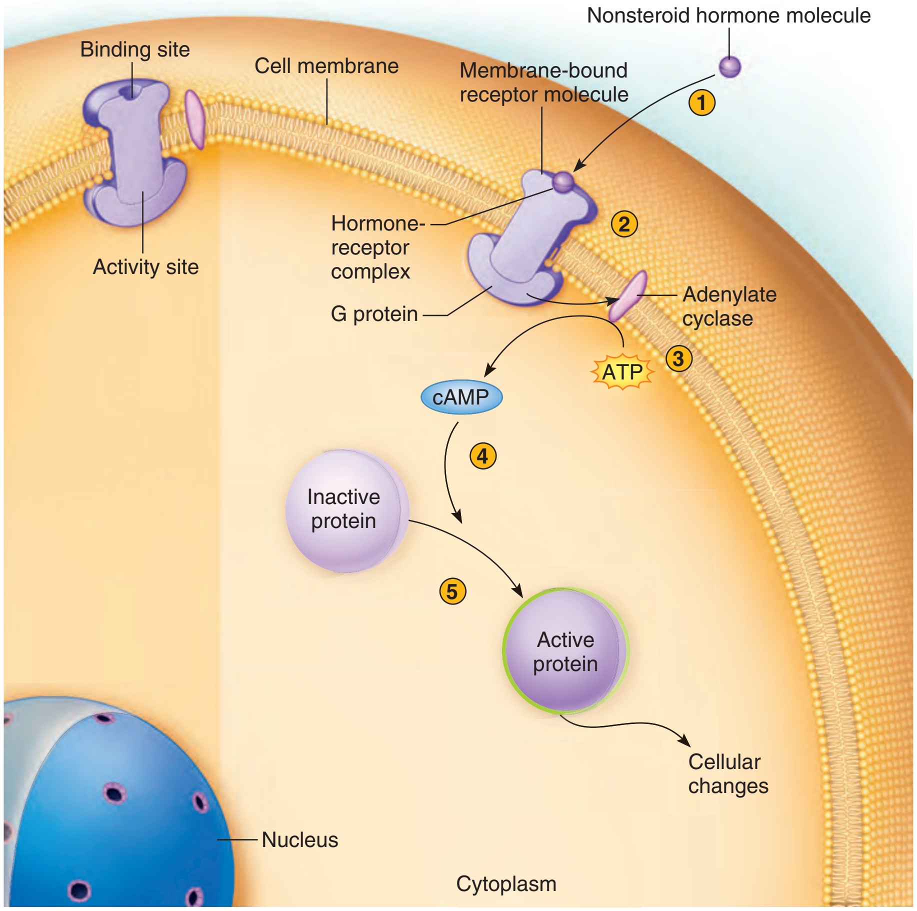
① A steroid hormone crosses a cell membrane

② The hormone combines with a protein receptor, usually in the nucleus

③ The hormone-receptor complex activates synthesis of specific messenger RNA (mRNA) molecules

④ The mRNA molecules leave the nucleus and enter the cytoplasm

⑤ Translation of mRNA molecules leads to synthesis of the encoded proteins which are associated with the hormone's action


Nonsteroid hormone molecule
Binding site
Cell membrane
Membrane-bound receptor molecule
①
Activity site
Hormone-receptor complex
②
G protein
Adenylate cyclase
ATP
③
cAMP
④
Inactive protein
⑤
Active protein
Cellular changes
Nucleus
Cytoplasm

① A nonsteroid hormone reaches a target cell

② Nonsteroid hormones bind receptor molecules on the cell membrane

③ Hormone binding activates molecules of adenylate cyclase

④ Adenylate cyclase catalyzes conversion of ATP into cyclic adenosine monophosphate (cAMP)

⑤ cAMP activates existing proteins, causing a series of reactions leading to the cellular changes associated with the hormone's action

**FIGURE 11.4** APR Nonsteroid hormone action.

The type of membrane receptors present and the kinds of protein substrate molecules in a cell determine the cell's response to a hormone. Such responses to second messenger activation include altering membrane permeabilities, activating enzymes, promoting synthesis of certain proteins, stimulating or inhibiting specific metabolic pathways, moving the cell, and initiating secretion of hormones or other substances.

Another enzyme (phosphodiesterase) quickly inactivates cAMP, so that its action is short-lived. For this reason, a continuing response of a target cell requires a continuing signal from hormone molecules binding the target cell's membrane receptors.

A number of other second messengers work in much the same way. These include diacylglycerol (DAG) and inositol triphosphate ($IP_3$).

Abnormal or missing G proteins cause a variety of disorders, including colorblindness, precocious puberty, retinitis pigmentosa, and several thyroid problems.

## Prostaglandins

A group of biochemicals called **prostaglandins** (pros″tah-glan′dinz) also regulates cells. Prostaglandins are lipids synthesized from a fatty acid (arachidonic acid) in cell membranes. A great variety of cells produce prostaglandins, including those of the liver, kidneys, heart, lungs, thymus, pancreas, brain, and reproductive organs. Prostaglandins usually act more locally than hormones, often affecting only the organ where they are produced.

Prostaglandins are potent and are present in very small amounts. They are not stored in cells, but rather synthesized just before release. They are rapidly inactivated.

Prostaglandins produce diverse and even opposite effects. Some prostaglandins, for example, relax smooth muscle in the airways of the lungs and in blood vessels, while others contract smooth muscle in the walls of the uterus and intestines. Prostaglandins stimulate hormone secretion from the adrenal cortex and inhibit secretion of hydrochloric acid from the stomach wall. They also influence the movements of sodium ions and water molecules in the kidneys, help regulate blood pressure, and have powerful effects on male and female reproductive physiology.

### PRACTICE

7. How does a steroid hormone promote cellular changes? How does a nonsteroid hormone do the same?
8. What is a second messenger?
9. What are prostaglandins?
10. What are the effects of prostaglandins?

## 11.4 Control of Hormonal Secretions

Hormones are continually excreted in the urine and broken down by various enzymes, primarily in the liver. Therefore, maintaining constant hormone levels requires ongoing hormone secretion. To increase or decrease the blood levels of a hormone, the body increases or decreases secretion. Not surprisingly, hormone secretion is precisely regulated.

Generally, hormone secretion is controlled in three ways, all of which use *negative feedback* (see chapter 1, p. 14). In each case, an endocrine gland or the system controlling it detects the concentration (blood level) of the hormone the gland secretes, a process the hormone controls, or an action the hormone has on the internal environment (fig. 11.5). The three mechanisms of hormone control are described below.

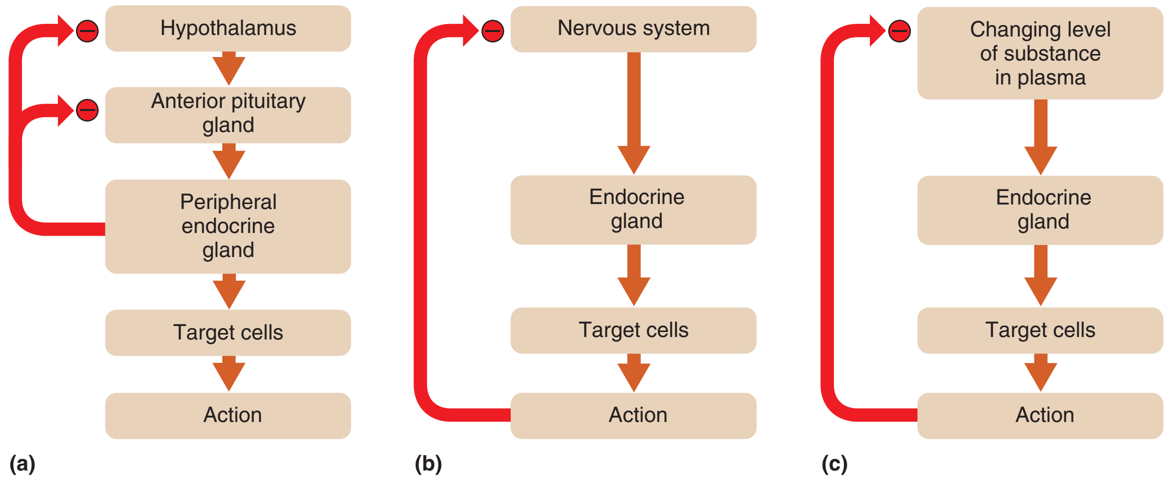


**FIGURE 11.5** Control of the endocrine system occurs in three ways: **(a)** The hypothalamus and anterior pituitary stimulate other endocrine glands; **(b)** the nervous system stimulates a gland directly; or **(c)** changes in the internal environment stimulate glands directly. (⊖ indicates negative feedback inhibition.)

1. The hypothalamus regulates the anterior pituitary gland's release of hormones that stimulate other endocrine glands to release hormones. Its location near the thalamus and the third ventricle allows the hypothalamus to constantly receive information about the internal environment from neural connections and cerebrospinal fluid (fig. 11.5*a*).
2. The nervous system stimulates some glands directly. The adrenal medulla, for example, secretes its hormones in response to sympathetic impulses (fig. 11.5*b*).
3. Another group of glands responds directly to changes in the composition of the internal environment. For example, when the blood glucose level rises, the pancreas secretes insulin, and when the blood glucose level falls, it secretes glucagon (fig. 11.5*c*).

In each of these cases, as hormone levels rise in the blood and the hormone exerts its effects, negative feedback inhibits the system, and hormone secretion decreases. Then, as hormone levels in the blood decrease and the hormone's effects are no longer taking place, inhibition of the system is lifted, and secretion of that hormone increases again. As a result of negative feedback, hormone levels in the bloodstream remain relatively stable, tending to fluctuate slightly above and below an average value (fig. 11.6).

## PRACTICE

11. Explain three examples of control of hormonal secretion.
12. Describe a negative feedback system that controls hormone secretion.

## 11.5 | Pituitary Gland

The **pituitary gland** (hypophysis) is located at the base of the brain, where a pituitary stalk (infundibulum) attaches it to the hypothalamus. The gland is about 1 centimeter in diameter and consists of an **anterior pituitary** (pĭ-tu′ĭ-tār″e), or anterior lobe, and a **posterior pituitary,** or posterior lobe (fig. 11.7).

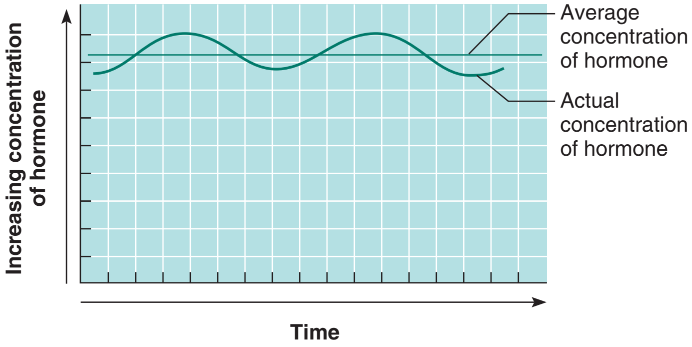


**FIGURE 11.6** As a result of negative feedback, hormone concentrations remain relatively stable, although they may fluctuate slightly above and below average concentrations.

In the fetus, a narrow region develops between the anterior and posterior lobes of the pituitary gland. Called the *intermediate lobe* (pars intermedia), it produces melanocyte-stimulating hormone (MSH), which regulates the synthesis of melanin—the pigment in skin and in parts of the eyes and brain. In most adults, this intermediate lobe is no longer a distinct structure, but its secretory cells persist in the two remaining lobes.

The brain controls most of the pituitary gland's activity. In fact, the posterior pituitary is actually part of the nervous system. Certain neurons whose cell bodies are in the hypothalamus have axons that extend down into the posterior pituitary gland. Impulses on their axons trigger the release of chemicals from their axon terminals, which then enter the bloodstream as posterior pituitary hormones (fig. 11.8).

The anterior pituitary consists of glandular cells rather than neurons, but it is still controlled by the brain. Axon terminals of another population of hypothalamic neurons release chemicals called **releasing hormones** (and some release-inhibiting hormones) into a capillary network associated with the hypothalamus. The capillaries merge to form the **hypophyseal portal veins,** which pass downward along the pituitary stalk and give rise to a capillary network in the anterior pituitary (fig. 11.8). Thus, the hypothalamus releases substances that the blood carries directly to the anterior pituitary.

Upon reaching the anterior pituitary, each of the hypothalamic hormones acts on a specific population of cells. Some of the resulting actions are inhibitory, but most stimulate the anterior pituitary to release hormones that stimulate secretions from peripheral endocrine glands. In many of these cases, important negative feedback regulates hormone levels in the bloodstream.

## PRACTICE

13. Where is the pituitary gland located?
14. Explain how the hypothalamus controls the secretory activity of the posterior and anterior lobes of the pituitary gland.

### Anterior Pituitary Hormones

The anterior pituitary is enclosed in a capsule of dense connective tissue and consists largely of epithelial tissue organized in blocks around many thin-walled blood vessels. So far researchers have identified five types of secretory cells in this epithelium. Four of these cell types each secrete a different hormone—growth hormone (GH), prolactin (PRL), thyroid-stimulating hormone (TSH), and adrenocorticotropic

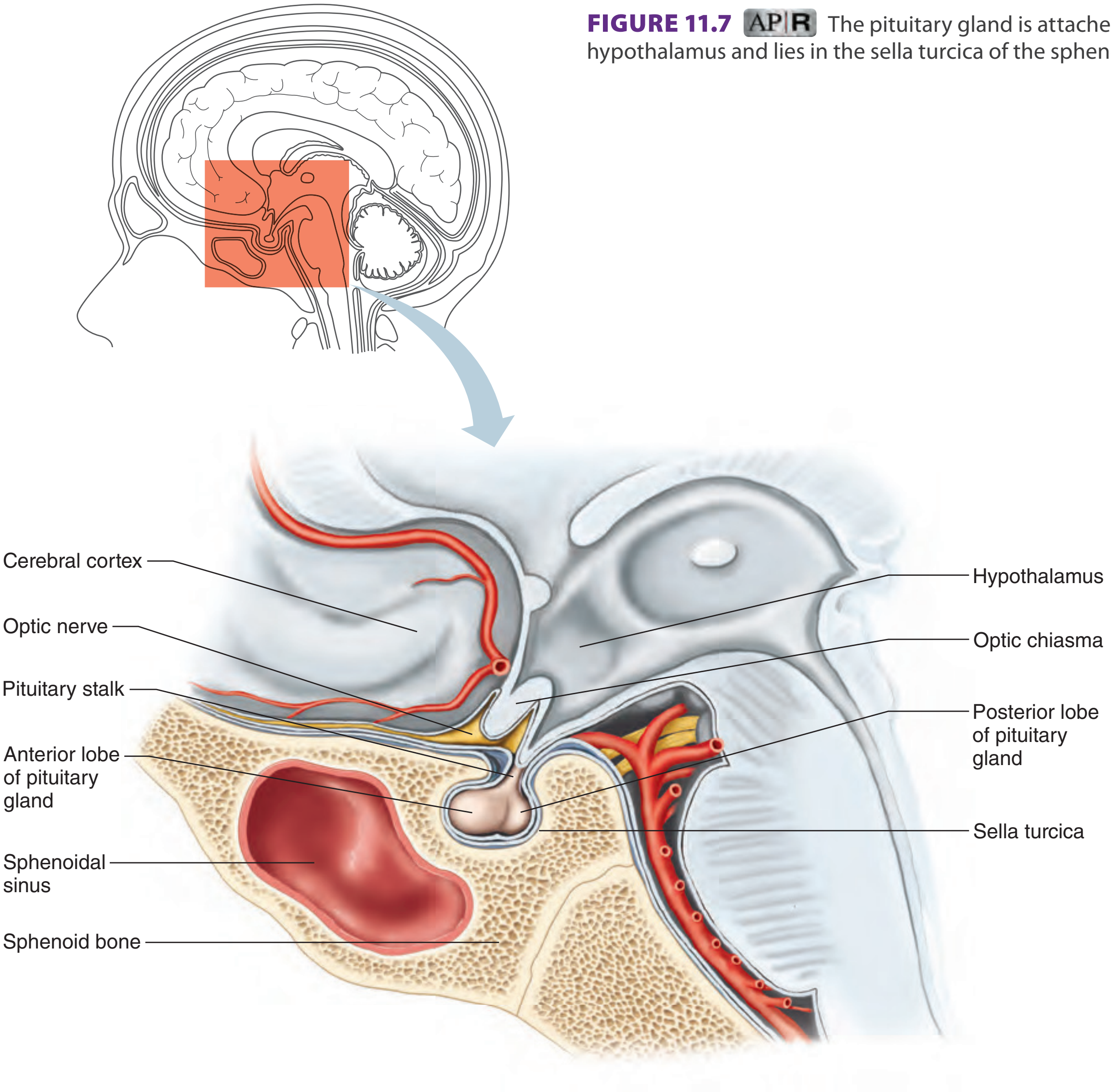


**FIGURE 11.7** APR The pituitary gland is attached to the hypothalamus and lies in the sella turcica of the sphenoid bone.

hormone (ACTH). The fifth type of cell secretes both follicle-stimulating hormone (FSH) and luteinizing hormone (LH). (In males, luteinizing hormone is sometimes referred to as interstitial cell stimulating hormone, or ICSH.)

**Growth hormone (GH)** stimulates cells to enlarge and divide more frequently. It also enhances the movement of amino acids across cell membranes and speeds the rate at which cells utilize carbohydrates and fats. The hormone's effect on amino acids is important in stimulating growth.

Two hormones from the hypothalamus control GH secretion: *GH-releasing hormone (GHRH)* and *GH release-inhibiting hormone (GHIH)*. Nutritional state also influences control of GH. For example, more GH is released during periods of protein deficiency and abnormally low blood glucose concentration. Conversely, when blood protein and glucose concentrations increase, GH secretion decreases.

Insufficient secretion of growth hormone (GH) during childhood limits growth, causing pituitary dwarfism. Body parts are normally proportioned, and mental development is normal—the individual is just very small. Typically, hormone therapy can stimulate some growth.

Oversecretion of GH during childhood causes gigantism, in which height may exceed 8 feet. This rare condition is usually a result of a pituitary gland tumor, which may also cause oversecretion of other pituitary hormones. As a result, a person with gigantism often has several metabolic disturbances.

Acromegaly is the overproduction of growth hormone in adulthood. The many symptoms attesting to the wide effects of this hormone include enlarged heart, bones, thyroid gland, facial features, hands, feet, and head. Early symptoms include headache, joint pain, fatigue, and depression.

**Prolactin** (pro-lak′tin) **(PRL)** stimulates and sustains a woman's milk production following the birth of

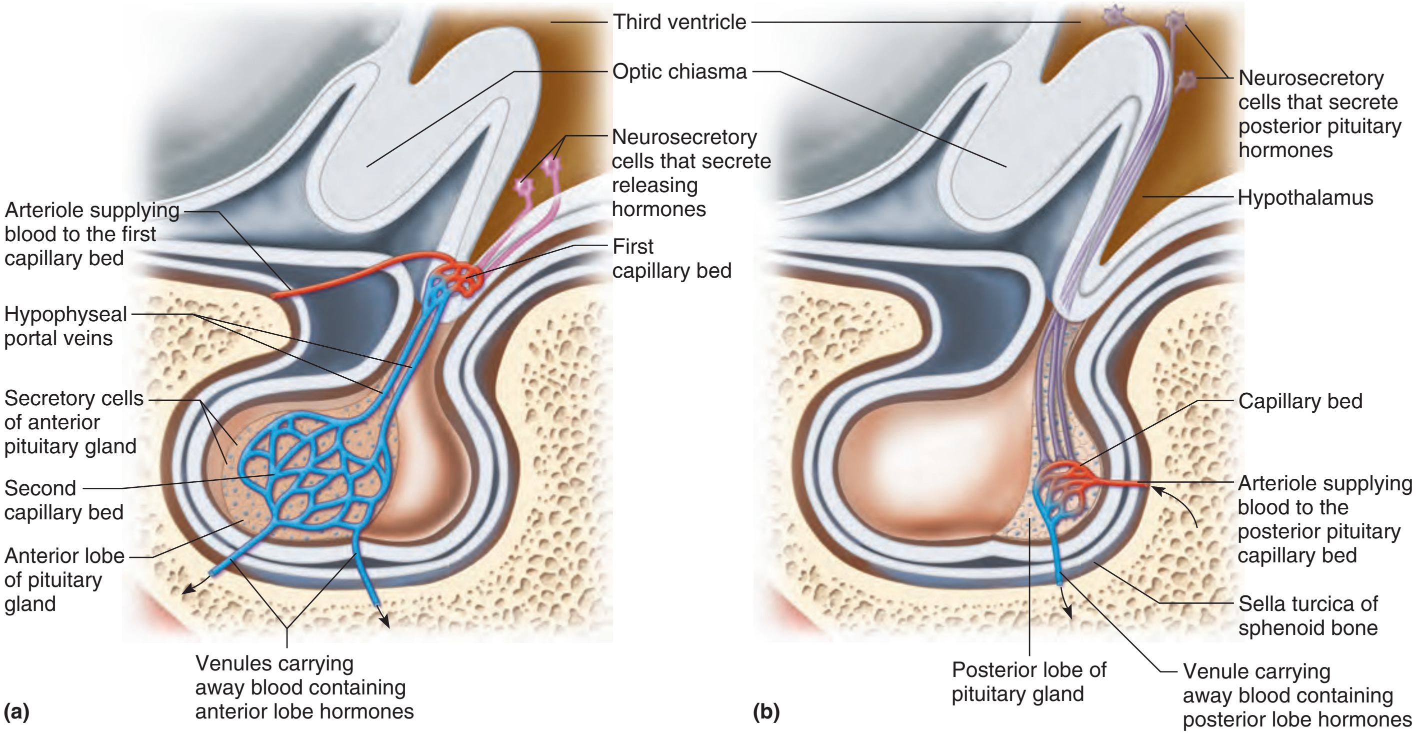

Third ventricle
Optic chiasma
Neurosecretory cells that secrete releasing hormones
First capillary bed
Arteriole supplying blood to the first capillary bed
Hypophyseal portal veins
Secretory cells of anterior pituitary gland
Second capillary bed
Anterior lobe of pituitary gland
Venules carrying away blood containing anterior lobe hormones
(a)
Neurosecretory cells that secrete posterior pituitary hormones
Hypothalamus
Capillary bed
Arteriole supplying blood to the posterior pituitary capillary bed
Sella turcica of sphenoid bone
Posterior lobe of pituitary gland
Venule carrying away blood containing posterior lobe hormones
(b)

**FIGURE 11.8** AP|R Secretion of pituitary hormones. **(a)** Releasing hormones from neurons in the hypothalamus stimulate secretory cells of the anterior lobe of the pituitary gland to secrete hormones. **(b)** Other neurons in the hypothalamus release their hormones directly into capillaries of the posterior lobe of the pituitary gland.

an infant (see chapter 20, p. 566). No normal physiological role in human males has been firmly established. Abnormally elevated levels of PRL can disrupt sexual function in both sexes.

**Thyroid-stimulating hormone (TSH)** controls thyroid gland secretions (described in section 11.6, on page 310). The hypothalamus partially regulates TSH secretion by producing *thyrotropin-releasing hormone (TRH)* (fig. 11.9). Circulating thyroid hormones inhibit release of TRH and TSH. As the blood concentration of thyroid hormones increases, secretion of TRH and TSH decreases.

**Adrenocorticotropic hormone** (ad-re″no-kor″te-ko-trōp′ik hor′mōn) **(ACTH)** controls the manufacture and secretion of certain hormones from the outer layer, or *cortex,* of the adrenal gland. (These hormones are discussed in section 11.8 on p. 315.) ACTH secretion is regulated in part by *corticotropin-releasing hormone (CRH),* which the hypothalamus releases in response to decreased concentrations of adrenal cortical hormones. Also, stress may increase ACTH secretion by stimulating the release of CRH.

**Follicle-stimulating hormone** (fol′ĭ-kl stim′u-la″ting hor′mōn) **(FSH)** and **luteinizing hormone** (lu′te-in-iz″ing hor′mōn) **(LH)** are *gonadotropins,* which means they exert their actions on the gonads, or reproductive organs. Gonads are the **testes** (tes′tēz) in the male and the **ovaries** (o′vah-rēz) in the female. (Chapter 19, pp. 528 and 535–536, discusses the functions of these gonadotropins and the ways they interact.)

## PRACTICE

15. How does growth hormone affect protein synthesis?
16. What is the function of prolactin?
17. How is secretion of thyroid-stimulating hormone regulated?
18. What is the function of adrenocorticotropic hormone?
19. What is a gonadotropin?

## Posterior Pituitary Hormones

The posterior pituitary consists mostly of axons and neuroglia, unlike the anterior pituitary, which is composed primarily of glandular epithelial cells. Neuroglia support the axons, which originate from neurons in the hypothalamus.

Specialized neurons in the hypothalamus produce the two hormones associated with the posterior pituitary—**antidiuretic hormone** (an″tĭ-di″u-ret′ik hor′mōn) **(ADH)** and **oxytocin** (ok″sĭ-to′sin) **(OT)** (see fig. 11.8). These hormones are transported down axons through the pituitary stalk to the posterior lobe, and are stored in vesicles (secretory granules) near the ends of the axons. Impulses from the hypothalamus release the hormones into the blood. Thus, though synthesized in the hypothalamus, posterior pituitary hormones are named for where they enter the bloodstream.

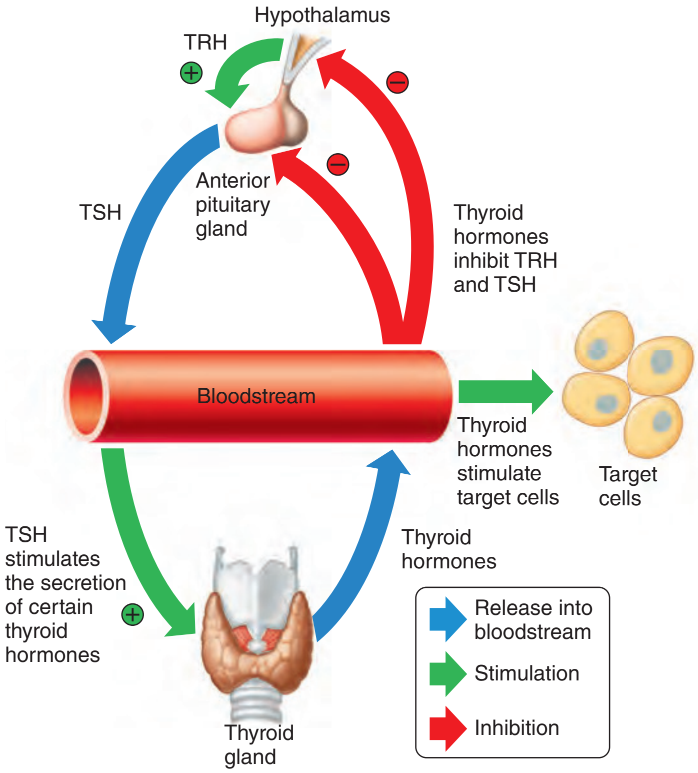


**FIGURE 11.9** Thyrotropin-releasing hormone (TRH) from the hypothalamus stimulates the anterior pituitary gland to release thyroid-stimulating hormone (TSH), which stimulates the thyroid gland to release hormones. These thyroid hormones reduce the secretion of TSH and TRH by negative feedback. (⊕ = stimulation; ⊖ = inhibition)

A *diuretic* is a chemical that increases urine production, whereas an *antidiuretic* decreases urine formation. ADH produces an antidiuretic effect by reducing the volume of water the kidneys excrete. In this way, ADH helps regulate the water concentration of body fluids.

The hypothalamus controls ADH secretion. Certain neurons in this part of the brain, called *osmoreceptors,* sense changes in the osmotic pressure of body fluids. Dehydration due to lack of water intake increasingly concentrates blood solutes. Osmoreceptors, sensing the resulting increase in osmotic pressure, signal the posterior pituitary to release ADH, which travels in the blood to the kidneys. As a result, the kidneys produce less urine, conserving water. On the other hand, drinking too much water dilutes body fluids, inhibiting ADH release. In response, the kidneys excrete more dilute urine until the water concentration of body fluids returns to normal.

If an injury or tumor damages any parts of the ADH-regulating mechanism, too little ADH may be synthesized or released, producing *diabetes insipidus*. An affected individual may produce as much as 20 liters of very dilute urine per day, and solute concentrations in body fluids rise.

OT contracts smooth muscle in the uterine wall and stimulates uterine contractions in the later stages of childbirth. Stretching of uterine and vaginal tissues late in pregnancy triggers OT release during childbirth. In the breast, OT contracts specialized cells (myoepithelial cells) associated with the milk-producing glands and their ducts. In lactating breasts, this action forces liquid from the milk glands into the milk ducts and ejects the milk from the breasts for breastfeeding. In addition, OT is an antidiuretic, but it is much weaker than ADH. Table 11.3 reviews the hormones of the pituitary gland.

If a pregnant woman near or at her "due date" has certain signs of the approaching birth, but is not yet experiencing uterine contractions (labor pains), she may be given a form of oxytocin to stimulate contractions. Oxytocin may also be administered to the mother following childbirth to contract the uterus sufficiently to squeeze broken blood vessels closed, minimizing the risk of hemorrhage.

### PRACTICE

20. What is the function of antidiuretic hormone?
21. How is secretion of antidiuretic hormone controlled?
22. What effects does oxytocin produce in females?

## 11.6 | Thyroid Gland

The **thyroid gland** (thi′roid gland) is a very vascular structure that consists of two large lobes connected by a broad *isthmus* (is′mus). It is bilateral, just inferior to the larynx and anterior to the trachea (fig. 11.10 and reference plate 4, p. 35).

### Structure of the Gland

A capsule of connective tissue covers the thyroid gland, which is made up of many secretory parts called *follicles.* The follicles have cavities that are lined with a single layer of cuboidal epithelial cells and filled with a clear, viscous substance called *colloid.* The follicular cells produce and secrete hormones that are either stored in the colloid or released into the blood in nearby capillaries.

### Thyroid Hormones

The follicular cells of the thyroid gland synthesize two hormones—**thyroxine** (thi-rok′sin) (tetraiodothyronine), also known as $T_4$ because it contains four atoms of iodine, and **triiodothyronine** (tri″i-o″do-thi′ro-nēn), known as $T_3$ because it includes three atoms of iodine. Thyroxine and triiodothyronine have similar actions,

## TABLE 11.3 Hormones of the Pituitary Gland

| Hormone | Action | Source of Control |
|---|---|---|
| *Anterior Lobe* | | |
| Growth hormone (GH) | Stimulates an increase in the size and division rate of body cells; enhances movement of amino acids across membranes | Growth hormone-releasing hormone and growth hormone release-inhibiting hormone from hypothalamus |
| Prolactin (PRL) | Sustains milk production after birth | Secretion restrained by prolactin release-inhibiting hormone and stimulated by prolactin-releasing factor from hypothalamus |
| Thyroid-stimulating hormone (TSH) | Controls secretion of hormones from thyroid gland | Thyrotropin-releasing hormone (TRH) from hypothalamus |
| Adrenocorticotropic hormone (ACTH) | Controls secretion of certain hormones from adrenal cortex | Corticotropin-releasing hormone (CRH) from hypothalamus |
| Follicle-stimulating hormone (FSH) | In females, responsible for the development of egg-containing follicles in ovaries and stimulates follicular cells to secrete estrogen; in males, stimulates production of sperm cells | Gonadotropin-releasing hormone from hypothalamus |
| Luteinizing hormone (LH) | Promotes secretion of sex hormones; plays a role in releasing an egg cell in females | Gonadotropin-releasing hormone from hypothalamus |
| *Posterior Lobe** | | |
| Antidiuretic hormone (ADH) | Causes kidneys to conserve water; in high concentration, increases blood pressure | Hypothalamus in response to changes in water concentration in body fluids |
| Oxytocin (OT) | Contracts smooth muscle in the uterine wall; contracts myoepithelial cells associated with milk-secreting glands | Hypothalamus in response to stretching of uterine and vaginal walls and stimulation of breasts |

*These hormones are synthesized in the hypothalamus, as explained in the text.

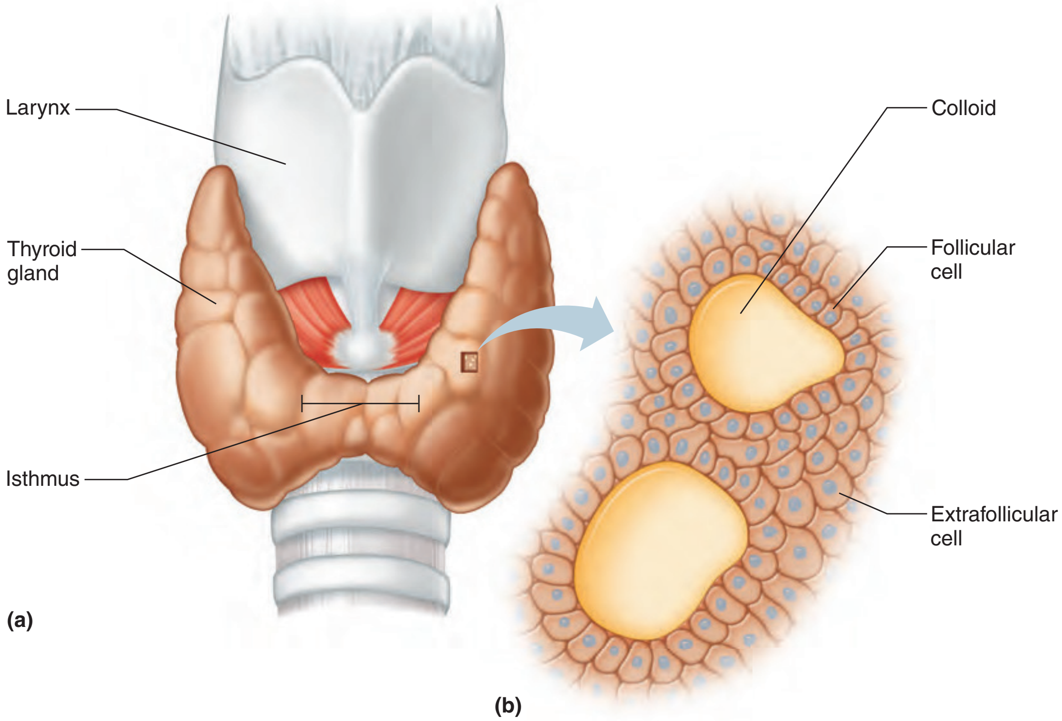


**FIGURE 11.10** APR Thyroid gland. **(a)** The thyroid gland consists of two lobes connected anteriorly by an isthmus. **(b)** Follicular cells secrete the thyroid hormones, thyroxine and triiodothyronine. Extrafollicular cells secrete calcitonin.

although triiodothyronine is five times more potent. These hormones help regulate the metabolism of carbohydrates, lipids, and proteins. They increase the rate at which cells release energy from carbohydrates, increase the rate of protein synthesis, and stimulate breakdown and mobilization of lipids. Thyroid hormones are the major factors determining how many calories the body must consume at rest in order to maintain life, which is known as the *basal metabolic rate (BMR)*. Thyroid hormones are required for normal growth and development, and are essential to nervous system maturation.

Follicular cells require iodine salts (iodides) to produce thyroxine and triiodothyronine. Foods normally provide iodides, and after the iodides have been absorbed from the intestine, blood transports them to the thyroid gland. An efficient active transport mechanism moves the iodides into the follicular cells, where they are used to synthesize the hormones. The hypothalamus and anterior pituitary gland control the synthesis and release of thyroid hormones. Once in the blood, thyroxine and triiodothyronine combine with proteins in the blood (plasma proteins) and are transported to body cells.

A third hormone of the thyroid gland, **calcitonin** (kal′sĭ-to′nin), is not referred to as “thyroid hormone” because it is produced by the thyroid’s extrafollicular (other than follicle) cells. Along with parathyroid hormone (PTH) from the parathyroid glands, calcitonin regulates the concentrations of blood calcium and phosphate ions (see fig. 7.8, p. 152).

The blood concentration of calcium ions regulates calcitonin release. As this concentration increases, so does calcitonin secretion. Calcitonin stimulates the bone-forming activity of osteoblasts (see chapter 7, p. 147), inhibits the bone-resorbing activity of osteoclasts (see chapter 7, p. 148), and increases the kidneys’ excretion of calcium and phosphate ions—actions that lower the blood calcium and phosphate ion concentrations. Table 11.4 reviews the actions and controls of the thyroid hormones.

**PRACTICE**

23. Where is the thyroid gland located?
24. Which hormones of the thyroid gland affect carbohydrate metabolism and protein synthesis?
25. How does the thyroid gland influence the concentrations of blood calcium and phosphate ions?

Thyroid disorders may produce underactivity (*hypothyroidism*) or overactivity (*hyperthyroidism*) of the glandular cells. One form of hypothyroidism, called cretinism, affects newborns because thyroid hormone provided during the pregnancy was insufficient. Symptoms include stunted growth, abnormal bone formation, slowed mental development, low body temperature, and sluggishness. Hypothyroidism is also common among older adults, producing fatigue and weight gain. Hyperthyroidism produces an elevated metabolic rate, restlessness, and overeating. The eyes protrude (exophthalmia) because of swelling in the tissues behind them, and the thyroid gland enlarges, producing a bulge in the neck called a *goiter*.

## 11.7 | Parathyroid Glands

The **parathyroid glands** (par″ah-thi′roid glandz) are on the posterior surface of the thyroid gland, as figure 11.11 shows. Most individuals have four parathyroid glands—a superior and an inferior gland associated with each of the thyroid’s lateral lobes.

### Structure of the Glands

A thin capsule of connective tissue covers each small, yellowish-brown parathyroid gland. The body of the gland consists of many tightly packed secretory cells closely associated with capillary networks.

### Parathyroid Hormone

The parathyroid glands secrete **parathyroid hormone (PTH),** which increases blood calcium concentration and decreases blood phosphate ion concentration. PTH affects the bones, kidneys, and intestine.

**TABLE 11.4** Hormones of the Thyroid Gland APR

| Hormone | Action | Source of Control |
|---|---|---|
| Thyroxine ($T_4$) | Increases rate of energy release from carbohydrates; increases rate of protein synthesis; accelerates growth; stimulates activity in nervous system | Thyroid-stimulating hormone from the anterior pituitary gland |
| Triiodothyronine ($T_3$) | Same as above, but five times more potent than thyroxine | Thyroid-stimulating hormone from the anterior pituitary gland |
| Calcitonin | Lowers blood calcium and phosphate ion concentrations by stimulating deposition of calcium and phosphate ions into bones, inhibiting release of these ions from bones, and by increasing excretion of these ions by kidneys | Blood calcium concentration |

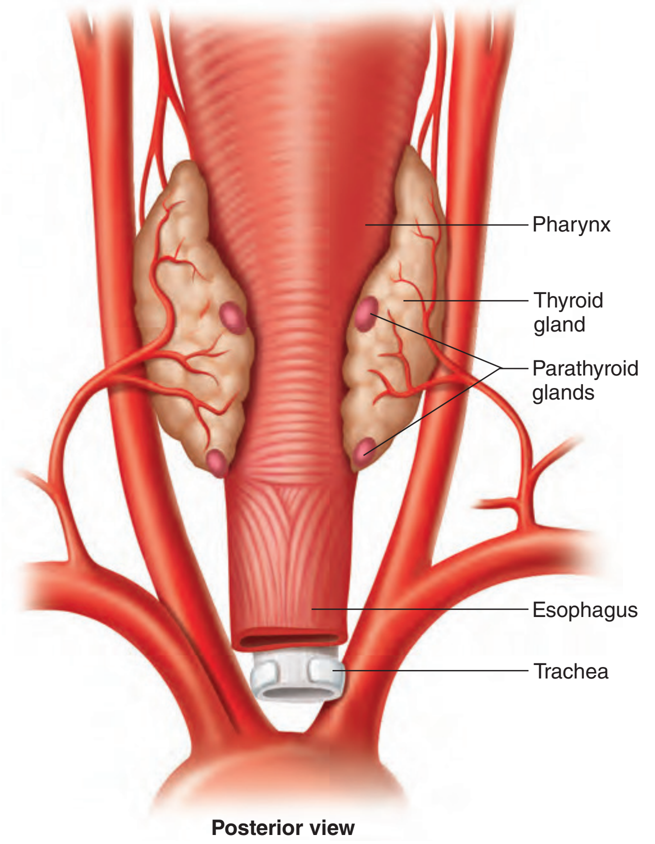

Pharynx
Thyroid gland
Parathyroid glands
Esophagus
Trachea
Posterior view

**FIGURE 11.11** The parathyroid glands are embedded in the posterior surface of the thyroid gland.

The extracellular matrix of bone tissue is rich in mineral salts, including calcium phosphate (see chapter 7, p. 152). PTH inhibits the activity of osteoblasts and stimulates osteoclasts to resorb bone and release calcium and phosphate ions into the blood. At the same time, PTH causes the kidneys to conserve blood calcium and to excrete more phosphate ions in the urine. It also stimulates calcium absorption from food in the intestine, further increasing blood calcium concentration.

Negative feedback between the parathyroid glands and the blood calcium concentration regulates PTH secretion. As blood calcium concentration drops, more PTH is secreted; as blood calcium concentration rises, less PTH is released (fig. 11.12).

To summarize, calcitonin and PTH activities maintain stable blood calcium concentration. Calcitonin decreases an above-normal blood calcium concentration, while PTH increases a below-normal blood calcium concentration (see fig. 7.8, p. 152).

## PRACTICE

26. Where are the parathyroid glands?
27. How does parathyroid hormone help regulate concentrations of blood calcium and phosphate ions?

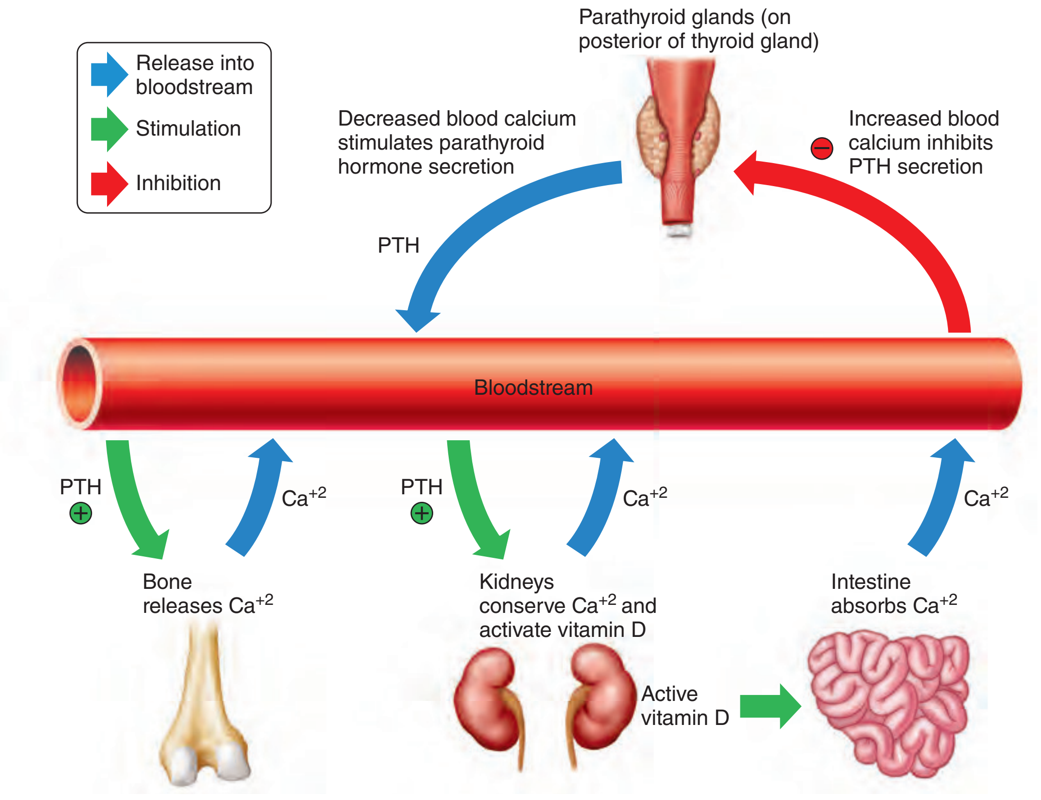

Release into bloodstream
Stimulation
Inhibition
Parathyroid glands (on posterior of thyroid gland)
Decreased blood calcium stimulates parathyroid hormone secretion
⊖ Increased blood calcium inhibits PTH secretion
PTH
Bloodstream
PTH ⊕
$Ca^{+2}$
PTH ⊕
$Ca^{+2}$
$Ca^{+2}$
Bone releases $Ca^{+2}$
Kidneys conserve $Ca^{+2}$ and activate vitamin D
Active vitamin D
Intestine absorbs $Ca^{+2}$

**FIGURE 11.12** APR Parathyroid hormone (PTH) stimulates bone to release calcium ($Ca^{+2}$) and the kidneys to conserve calcium. It indirectly stimulates the intestine to absorb calcium. The resulting increase in blood calcium concentration inhibits secretion of PTH by negative feedback. (⊕ = stimulation; ⊖ = inhibition)

Injury to the parathyroids or their surgical removal can cause *hypoparathyroidism,* in which decreased PTH secretion reduces osteoclast activity. Although the bones remain strong, the blood calcium concentration decreases. The nervous system may become abnormally excitable, triggering spontaneous impulses. As a result, muscles may undergo tetanic contractions, possibly leading to respiratory failure and death.

A tumor in a parathyroid gland may cause *hyperparathyroidism,* which increases PTH secretion. This stimulates osteoclast activity, and as bone tissue is resorbed, the bones soften, deform, and more easily fracture spontaneously. In addition, excess calcium and phosphate released into body fluids may be deposited in abnormal places, causing new problems, such as kidney stones.

## 11.8 | Adrenal Glands

The **adrenal glands** (ah-dre′nal glandz) are closely associated with the kidneys (fig. 11.13 and reference plate 6, p. 37). A gland sits atop each kidney like a cap and is embedded in the mass of adipose tissue that encloses the kidney.

### Structure of the Glands

Each adrenal gland is very vascular and consists of two parts: The central portion is the **adrenal medulla** (ah-dre′nal me-dul′ah), and the outer part is the **adrenal cortex** (ah-dre′nal kor′teks). These regions are not sharply divided, but they are functionally distinct structures that secrete different hormones.

The adrenal medulla consists of irregularly shaped cells organized in groups around blood vessels. These cells are intimately connected with the sympathetic division of the autonomic nervous system. Adrenal medullary cells are actually modified postganglionic neurons. Preganglionic autonomic nerve fibers lead to them from the central nervous system (see chapter 9, pp. 262–263).

The adrenal cortex, which makes up the bulk of the adrenal gland, is composed of closely packed masses of epithelial cells, organized in layers. These layers form an outer (glomerulosa), middle (fasciculata), and inner (reticularis) zone of the cortex (fig. 11.13*b*). As in the adrenal medulla, the cells of the adrenal cortex are well supplied with blood vessels.

**PRACTICE**

28. Where are the adrenal glands?
29. Describe the two portions of an adrenal gland.

### Hormones of the Adrenal Medulla

The cells of the adrenal medulla secrete two closely related hormones—**epinephrine** (ep″ĭ-nef′rin) (adrenalin) and **norepinephrine** (nor″ep-ĭ-nef′rin) (noradrenalin). These hormones have similar molecular structures

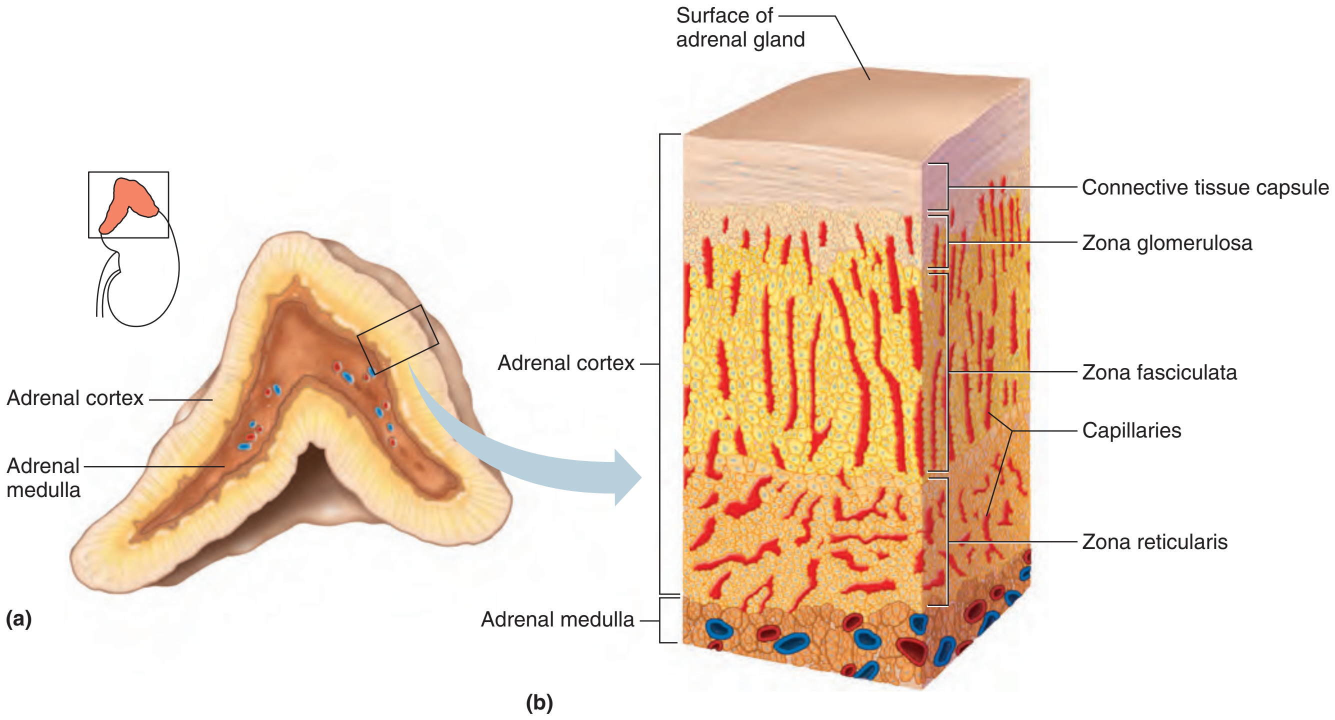


**FIGURE 11.13** APR Adrenal glands. **(a)** An adrenal gland consists of an outer cortex and an inner medulla. **(b)** The cortex consists of three layers, or zones, of cells.

and physiological functions. In fact, epinephrine, which makes up 80% of the adrenal medullary secretion, is synthesized from norepinephrine.

The effects of the adrenal medullary hormones resemble those of sympathetic neurons stimulating their effectors. Hormonal effects, however, last up to ten times longer because hormones are broken down more slowly than neurotransmitters. Epinephrine and norepinephrine increase heart rate, the force of cardiac muscle contraction, breathing rate, and blood glucose level. They also elevate blood pressure and decrease digestive activity.

Impulses arriving on sympathetic nerve fibers stimulate the adrenal medulla to release its hormones at the same time that sympathetic impulses are stimulating other effectors. These sympathetic impulses originate in the hypothalamus in response to stress. In this way, adrenal medullary secretions function with the sympathetic division of the autonomic nervous system in preparing the body for energy-expending action, also called “fight-or-flight responses.” Table 11.5 compares some of the effects of the adrenal medullary hormones.

Tumors in the adrenal medulla can increase hormonal secretion. Release of norepinephrine usually predominates, prolonging sympathetic responses—high blood pressure, increased heart rate, elevated blood sugar, and so forth. Surgical removal of the tumor corrects the condition.

**PRACTICE**

30. Name the hormones the adrenal medulla secretes.
31. What effects do hormones from the adrenal medulla produce?
32. What stimulates release of hormones from the adrenal medulla?

## Hormones of the Adrenal Cortex

The cells of the adrenal cortex produce more than thirty different steroids, including several hormones. Unlike the adrenal medullary hormones, without which a person can still survive, some adrenal cortical hormones are vital. Without extensive electrolyte therapy a person usually dies within a week. The most important adrenal cortical hormones are aldosterone, cortisol, and certain sex hormones.

### *Aldosterone*

Cells in the outer zone of the adrenal cortex synthesize **aldosterone** (al-dos′ter-ōn″). This hormone is a *mineralocorticoid* (min″er-al-o-kor′tĭ-koid) because it helps regulate the concentration of mineral electrolytes. More specifically, aldosterone causes the kidney to conserve sodium ions and excrete potassium ions. By conserving sodium ions, aldosterone stimulates water retention indirectly by osmosis, helping to maintain blood volume and blood pressure.

A decrease in the blood concentration of sodium ions or an increase in the blood concentration of potassium ions stimulates the cells that secrete aldosterone. The kidneys also indirectly stimulate aldosterone secretion if blood pressure falls.

### *Cortisol*

**Cortisol** (kor′tĭ-sol) (hydrocortisone) is a *glucocorticoid* (gloo″ko-kor′tĭ-koid), which means it affects glucose metabolism. It is produced in the middle zone of the adrenal cortex and, like aldosterone, is a steroid. Cortisol also influences protein and fat metabolism.

The more important actions of cortisol include:

1. Inhibition of protein synthesis in tissues, increasing the blood concentration of amino acids.

**TABLE 11.5 Comparative Effects of Epinephrine and Norepinephrine**

| Structure or function affected | Epinephrine | Norepinephrine |
|---|---|---|
| Heart | Rate increases<br>Force of contraction increases | Rate increases<br>Force of contraction increases |
| Blood vessels | Vasodilation, especially important in skeletal muscle at onset of fight-or-flight response | Vasoconstriction in skin and viscera shifts blood flow to other areas, such as exercising skeletal muscle |
| Systemic blood pressure | Some increase due to increased cardiac output | Some increase due to increased cardiac output and vasoconstriction (offset in some areas, such as exercising skeletal muscle, by local vasodilation due to other factors) |
| Airways | Dilation | Some dilation |
| Reticular formation of brainstem | Activated | Little effect |
| Liver | Promotes breakdown of glycogen to glucose, increasing blood sugar concentration | Little effect on blood glucose level |
| Metabolic rate | Increases | Increases |

2. Promotion of fatty acid release from adipose tissue, increasing the utilization of fatty acids as an energy source and decreasing the use of glucose.
3. Stimulation of liver cells to synthesize glucose from noncarbohydrates, such as circulating amino acids and glycerol, increasing the blood glucose concentration.

These actions of cortisol help keep blood glucose concentration within the normal range between meals, because a few hours without food can exhaust the supply of liver glycogen, a major source of glucose.

Negative feedback controls cortisol release. This is much like control of thyroid hormones, involving the hypothalamus, anterior pituitary gland, and adrenal cortex. The hypothalamus secretes corticotropin-releasing hormone (CRH) into the hypophyseal portal veins, which carry CRH to the anterior pituitary, stimulating it to secrete ACTH. In turn, ACTH stimulates the adrenal cortex to release cortisol. Cortisol inhibits the release of CRH and ACTH, and as concentrations of these fall, cortisol production drops (fig. 11.14).

The set point of the feedback mechanism controlling cortisol secretion changes from time to time, altering hormone output to meet the demands of changing conditions. For example, under stress—as from injury, disease, extreme temperature, or emotional upset—information reaches the brain concerning the stressful condition. In response, brain centers signal the hypothalamus to release more CRH, elevating cortisol concentration until the stress subsides (fig. 11.14).

### *Adrenal Sex Hormones*

Cells in the inner zone of the adrenal cortex produce sex hormones. These hormones are male types (adrenal androgens), but some are converted to female hormones (estrogens) in the skin, liver, and adipose tissue. Adrenal sex hormones may supplement the supply of sex hormones from the gonads and stimulate early development of reproductive organs. Table 11.6 summarizes the characteristics of the adrenal cortical hormones.

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Hyposecretion of adrenal cortical hormones leads to *Addison disease,* a condition characterized by decreased blood sodium, increased blood potassium, low blood glucose concentration (hypoglycemia), dehydration, low blood pressure, and increased skin pigmentation. Without treatment with mineralocorticoids and glucocorticoids, Addison disease can be lethal in days because of severe disturbances in electrolyte balance.

Hypersecretion of adrenal cortical hormones, which may be associated with an adrenal tumor or with the anterior pituitary oversecreting ACTH, causes *Cushing syndrome*. This condition alters carbohydrate and protein metabolism and electrolyte balance. For example, when mineralocorticoids and glucocorticoids are overproduced, blood glucose concentration remains high as glucose is synthesized from amino acids, depleting tissue protein. Also, too much sodium is retained, increasing tissue fluids, and the skin becomes puffy. At the same time, increase in adrenal sex hormone production may cause masculinizing effects in a female, such as beard growth and deepening of the voice.

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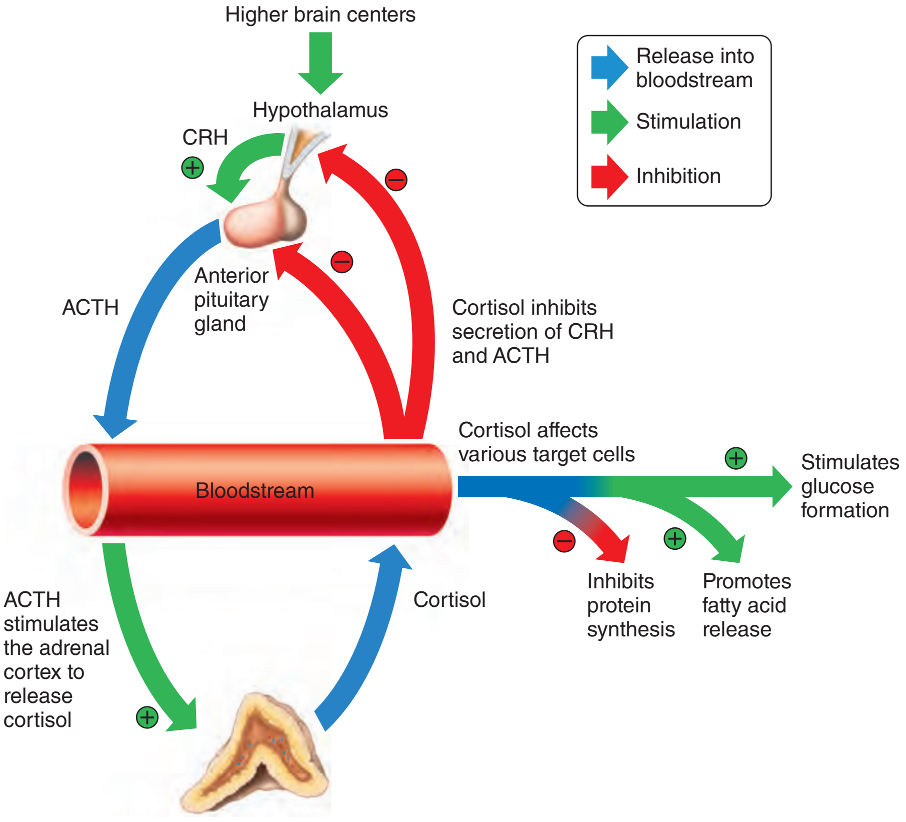

Higher brain centers
Hypothalamus
CRH
⊕
⊖
Release into bloodstream
Stimulation
Inhibition
⊖
Anterior pituitary gland
ACTH
Cortisol inhibits secretion of CRH and ACTH
Cortisol affects various target cells
⊕
Stimulates glucose formation
Bloodstream
⊖
⊕
Inhibits protein synthesis
Promotes fatty acid release
ACTH stimulates the adrenal cortex to release cortisol
⊕
Cortisol

**FIGURE 11.14** Negative feedback regulates cortisol secretion, similar to the regulation of thyroid hormone secretion.
⊕ = stimulation;
⊖ = inhibition)

**TABLE 11.6 Hormones of the Adrenal Cortex**

| Hormone | Action | Factor Regulating Secretion |
|---|---|---|
| Aldosterone | Helps regulate concentration of extracellular electrolytes by conserving sodium ions and excreting potassium ions | Sodium and potassium concentrations in body fluids |
| Cortisol | Decreases protein synthesis, increases fatty acid release, and stimulates glucose synthesis from noncarbohydrates | Corticotropin-releasing hormone from the hypothalamus and adrenocorticotropic hormone from the anterior pituitary |
| Adrenal androgens | Supplement sex hormones from the gonads; may be converted to estrogens in females | |

### PRACTICE

33. Name the most important hormones of the adrenal cortex.
34. What is the function of aldosterone?
35. What actions does cortisol produce?
36. How are the blood concentrations of aldosterone and cortisol regulated?

## 11.9 | Pancreas

The **pancreas** (pan′kre-as) consists of two major types of secretory tissues. This reflects the pancreas's dual function as an exocrine gland that secretes digestive juice and an endocrine gland that releases hormones (fig. 11.15 and reference plate 6, p. 37). The dual nature of the pancreas begins in the embryo. First, ducts form whose walls harbor progenitor cells (see fig. 3.23, p. 82). Some of the progenitor cells divide to yield daughter cells that specialize as exocrine cells, and others divide to yield cells that differentiate into endocrine cells. The two functions are elaborated as the gland develops further.

### Structure of the Gland

The pancreas is an elongated, somewhat flattened organ posterior to the stomach and behind the parietal peritoneum. A duct joins the pancreas to the duodenum (the first section of the small intestine). Digestive juice, the exocrine secretion of the pancreas, flows through this duct to the intestine. Chapter 15 (p. 423) discusses the digestive functions of the pancreas.

The endocrine part of the pancreas consists of groups of cells that are closely associated with blood vessels. These groups form "islands" of cells called *pancreatic islets* (islets of Langerhans) (figs. 11.15 and 11.16). The pancreatic islets include two distinct types of cells—alpha cells, which secrete the hormone glucagon, and beta cells, which secrete the hormone insulin. Clinical Application 11.1 discusses diabetes mellitus, a disorder that affects the beta cells.

### Hormones of the Pancreatic Islets

**Glucagon** (gloo′kah-gon) stimulates the liver to break down glycogen and convert certain noncarbohydrates, such as amino acids, into glucose, raising blood sugar concentration. Glucagon much more effectively elevates blood glucose than does epinephrine.

A negative feedback system regulates glucagon secretion. Low blood glucose concentration stimulates alpha cells to release glucagon. When blood

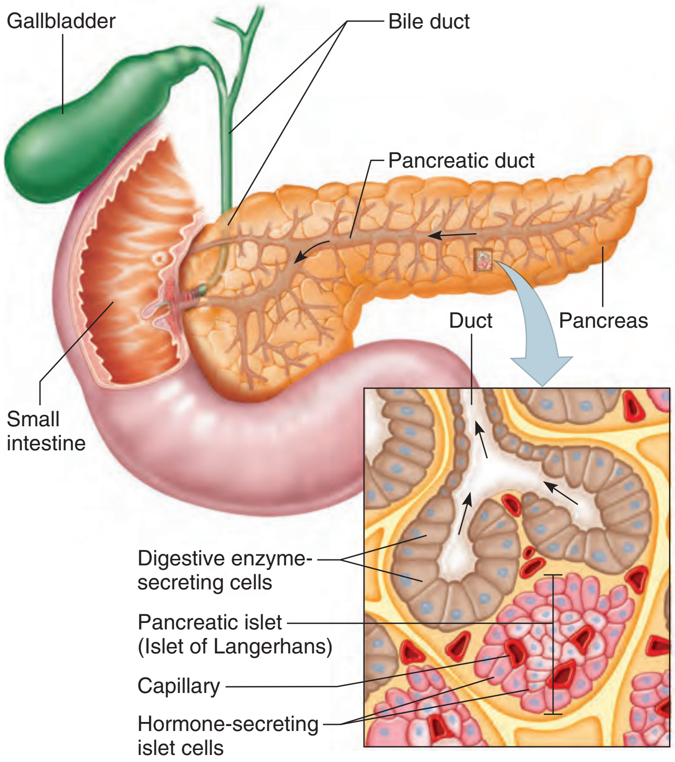

Gallbladder
Bile duct
Pancreatic duct
Duct
Pancreas
Small intestine
Digestive enzyme-secreting cells
Pancreatic islet (Islet of Langerhans)
Capillary
Hormone-secreting islet cells

**FIGURE 11.15** The hormone-secreting cells of the pancreas are grouped in clusters, or islets, that are in close proximity to blood vessels. Other pancreatic cells secrete digestive enzymes into ducts.

Q *What term describes the secretions that enter the pancreatic duct?*

**Answer can be found in Appendix F on page 582.**

CLINICAL APPLICATION 11.1

## Diabetes Mellitus

Diabetes mellitus is a metabolic disease that arises from lack of insulin or inability of cells to recognize insulin. Persistent elevated blood glucose affects the eyes, heart, kidneys, and peripheral nerves.

Insulin deficiency, or an impaired insulin response, disturbs carbohydrate, protein, and fat metabolism. Because insulin helps glucose cross some cell membranes, diabetes impairs movement of glucose into adipose and resting skeletal muscle cells. At the same time, formation of glycogen, which is a long chain of glucose molecules, declines. As a result, blood sugar concentration rises (hyperglycemia). When it reaches a certain level, the kidneys begin to excrete the excess. Glucose in the urine (glycosuria) raises the urine's osmotic pressure, and too much water is excreted. Excess urine output causes dehydration and extreme thirst (polydipsia).

Diabetes mellitus also hampers protein and fat synthesis. Glucose-starved cells increasingly use proteins for energy, and as a result, tissues waste away as weight drops, hunger increases, exhaustion becomes overwhelming, children stop growing, and wounds do not heal. Changes in fat metabolism cause fatty acids and ketone bodies to accumulate in the blood, which lowers pH (acidosis). Dehydration and acidosis may harm brain cells, causing disorientation, coma, and, eventually, death.

The two most common forms of diabetes mellitus are type 1 (insulin-dependent or juvenile diabetes) and type 2 (non-insulin-dependent or maturity-onset diabetes).

### Type 1 Diabetes Mellitus

Type 1 diabetes mellitus usually appears before age twenty. It is an autoimmune disease: the immune system destroys the beta cells of the pancreas (see chapter 14, p. 404).

People with type 1 diabetes must carefully monitor their blood glucose levels. They do this in two ways. Every three months, a laboratory test checks the levels of hemoglobin molecules in the blood that bind glucose. This measurement is called "A1C," and should be between 6% and 7%. A1C represents blood glucose level over the preceding three months, which is the lifespan of the red blood cells that transport hemoglobin. The second type of test is self-monitoring of blood glucose. A person uses a test kit to draw a drop of blood, applies it to a test strip, then uses a meter to read the concentration of glucose in the blood (in milligrams per deciliter). Normal plasma levels of glucose should range from 90 to 130 mg/dL before meals and less than 180 mg/dL one to two hours after meals. Most people with type 1 diabetes check their glucose this way two to four times a day. Smartphone apps record blood glucose levels with foods eaten and exercise done during the testing period.

Delivery of insulin to treat type 1 diabetes mimics normal pancreatic function (fig. 11A). People with type 1 diabetes inject insulin once or several times a day, or receive the hormone from an implanted insulin pump. Delivery of insulin through nasal sprays or skin patches is experimental. Replacing a diabetic pancreas with a healthy transplanted organ is difficult, the supply of

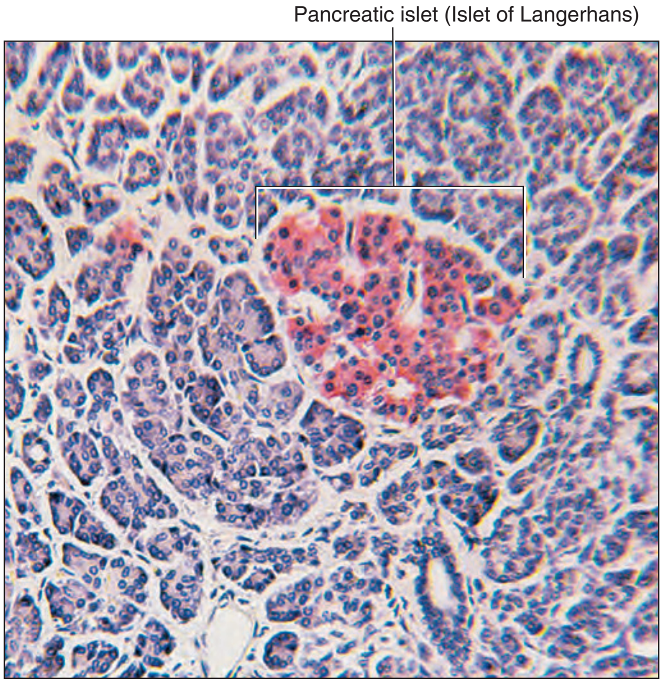


**FIGURE 11.16** APR Light micrograph of a pancreatic islet (250×).

glucose concentration rises, glucagon secretion falls. This control prevents hypoglycemia when glucose concentration is relatively low, such as between meals, or when glucose is used rapidly, such as during periods of exercise.

The main effect of **insulin** (in′su-lin) is exactly opposite that of glucagon. Insulin stimulates the liver to form glycogen from glucose and inhibits conversion of noncarbohydrates into glucose. Insulin also has the special effect of promoting facilitated diffusion (see chapter 3, p. 73) of glucose across cell membranes that have insulin receptors, such as those of adipose tissue, cardiac muscle, and skeletal muscle. (Glucose uptake by active skeletal muscle does not require insulin.) These actions of insulin decrease blood glucose concentration. In addition, insulin secretion promotes transport of amino acids into cells, increases the rate of protein synthesis, and stimulates adipose cells to synthesize and store fat.

A negative feedback system sensitive to blood glucose concentration regulates insulin secretion. When blood glucose concentration is high, such as after a

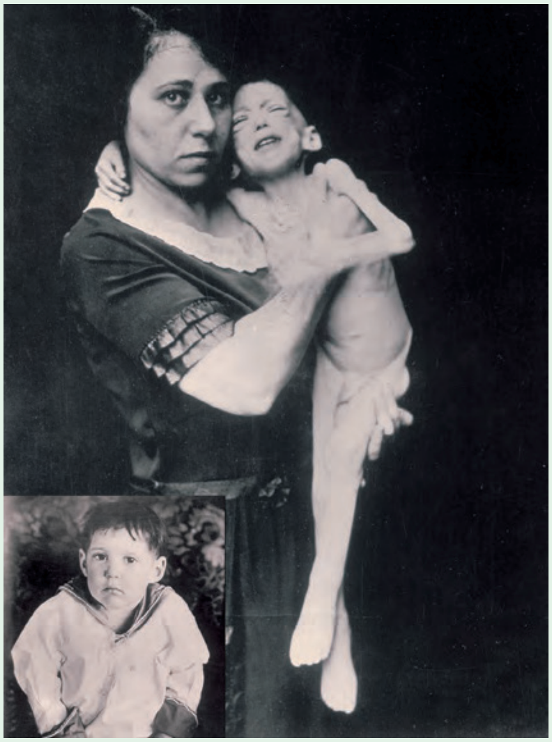


**FIGURE 11A** Before and after insulin treatment: The boy in his mother's arms is three years old but weighs only 15 pounds because of type 1 diabetes mellitus. The inset shows the same child after just two months of receiving insulin—his weight had doubled.

organs very limited, and immune rejection possible. Instead, research has focused on islet transplantation, which can decrease the need for insulin supplements for a few years.

### Type 2 Diabetes Mellitus

About 85–90% of people with diabetes mellitus have type 2, in which the beta cells produce insulin but body cells lose the ability to recognize it. The condition usually has milder symptoms than type 1 diabetes. Most affected individuals are overweight when symptoms begin. Treatment includes a low-carbohydrate, high-protein diet, aerobic and weight-bearing exercise, and maintaining a desirable body weight. Several oral drugs can help control glucose levels, which can delay the onset of diabetes-related complications. Weight loss surgery, including procedures that remove access to part of the digestive tract, can lower blood glucose significantly.

People with any type of diabetes must monitor and regulate their blood glucose level to forestall complications, which include coronary artery disease, peripheral nerve damage, and retinal damage. Evidence suggests that complications may begin even before blood glucose level indicates disease. The American Diabetes Association recognizes "pre-diabetes" as blood glucose levels above the normal range but not yet indicative of type 2 diabetes. About 20 million people in the United States between the ages of forty and seventy-four fall into this category.

meal, beta cells release insulin. Insulin helps prevent too high a blood glucose concentration by promoting glycogen formation in the liver and entrance of glucose into adipose and muscle cells. When glucose concentration falls, such as between meals or during the night, insulin secretion decreases.

As insulin output decreases, less and less glucose enters adipose and muscle cells. Cells that lack insulin receptors, such as nerve cells, can then use the glucose that remains in the blood. At the same time that insulin is decreasing, glucagon secretion is increasing. Therefore, insulin and glucagon are coordinated to maintain a relatively stable blood glucose concentration, despite great variation in the amount of carbohydrates a person eats (fig. 11.17).

Nerve cells, including those of the brain, obtain glucose by a facilitated diffusion mechanism that does not require insulin, but rather depends only on the blood glucose concentration. For this reason, nerve cells are particularly sensitive to changes in blood glucose concentration, and conditions that cause such changes—oversecretion of insulin leading to decreased blood glucose, for example—are likely to affect brain functions.

Cancer cells that develop from nonendocrine tissues sometimes inappropriately synthesize and secrete great amounts of peptide hormones or peptide hormonelike chemicals. For example, in endocrine paraneoplastic syndrome, a person with a non-endocrine cancer overproduces ADH, ACTH, a PTH-like substance, or an insulin-like substance.

## PRACTICE

37. What is the endocrine portion of the pancreas called?
38. What is the function of glucagon?
39. What is the function of insulin?
40. How are glucagon and insulin secretion controlled?
41. Why are nerve cells particularly sensitive to changes in blood glucose concentration?

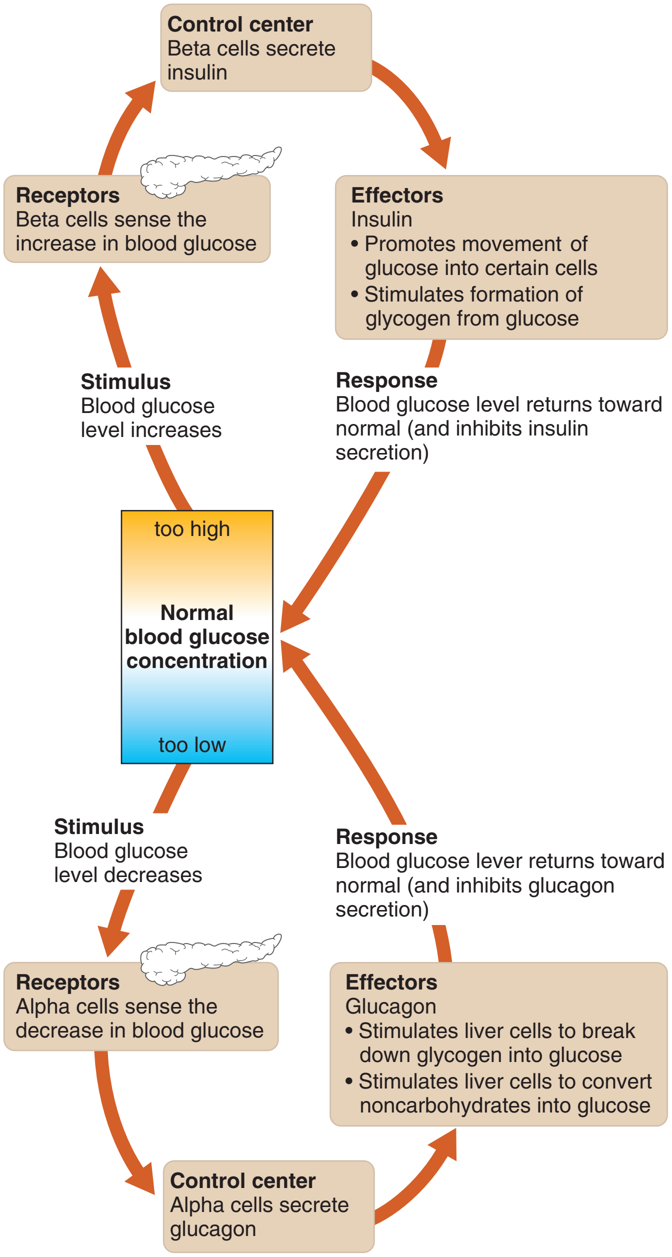

Control center
Beta cells secrete insulin
Receptors
Beta cells sense the increase in blood glucose
Effectors
Insulin
• Promotes movement of glucose into certain cells
• Stimulates formation of glycogen from glucose
Stimulus
Blood glucose level increases
Response
Blood glucose level returns toward normal (and inhibits insulin secretion)
too high
Normal blood glucose concentration
too low
Stimulus
Blood glucose level decreases
Response
Blood glucose lever returns toward normal (and inhibits glucagon secretion)
Receptors
Alpha cells sense the decrease in blood glucose
Effectors
Glucagon
• Stimulates liver cells to break down glycogen into glucose
• Stimulates liver cells to convert noncarbohydrates into glucose
Control center
Alpha cells secrete glucagon

**FIGURE 11.17** APR Insulin and glucagon function together to help maintain a relatively stable blood glucose concentration. Negative feedback responding to blood glucose concentration controls the levels of both hormones.

## 11.10 | Other Endocrine Glands

Other glands that produce hormones and thus are parts of the endocrine system include the pineal gland, the thymus, reproductive organs, and certain glands of the digestive tract, heart, and kidneys.

The **pineal gland** (pin′e-al gland) is a small structure located deep between the cerebral hemispheres, where it attaches to the upper part of the thalamus near the roof of the third ventricle (see fig. 11.2). The pineal gland secretes the hormone **melatonin** (mel″ah-to′nin) in response to light conditions outside the body. Impulses originating in the retinas of the eyes are conducted along axons that reach the pineal gland. In the dark, fewer impulses occur and melatonin secretion increases.

Melatonin acts on certain brain regions that function as a "biological clock," and may thereby help to regulate **circadian rhythms** (ser″kah-de′an rithmz), which are patterns of repeated activity associated with the environmental cycles of day and night. The changing levels of melatonin throughout the 24-hour day may enable the body to distinguish day from night. Circadian rhythms include the sleep–wake rhythm and seasonal cycles of fertility in many mammals. Clinical Application 11.2 discusses biological rhythms.

The fact that melatonin secretion responds to day length explains why traveling across several time zones produces the temporary insomnia of jet lag. Some clinical trials have found that taking melatonin 30 minutes before bedtime in the new location, for several days, hastens return to a normal sleep schedule, decreases daytime fatigue, and increases alertness. Studies have found that melatonin helps about half of people who take it for jet lag.

The mechanism of melatonin action is poorly understood, but the hormone inhibits the secretion of gonadotropins from the anterior pituitary and may help regulate the female reproductive cycle. It may also control the onset of puberty.

The **thymus** (thi′mus), which lies in the mediastinum posterior to the sternum and between the lungs, is relatively large in young children but shrinks with age (see fig. 11.2). This gland secretes a group of hormones called **thymosins** (thi′mo-sinz) that affect the production and differentiation of certain white blood cells (lymphocytes). In this way, the thymus plays an important role in immunity, discussed in chapter 14 (p. 392).

The reproductive organs that secrete important hormones include the testes, which produce testosterone; the ovaries, which produce estrogens and progesterone; and the **placenta** (plah-sen′tah), which produces estrogens, progesterone, and gonadotropin. These glands and their secretions are discussed in chapter 19 (pp. 520 and 534) and chapter 20 (p. 556).

The digestive glands that secrete hormones are associated with the linings of the stomach and small intestine. Chapter 15 (pp. 422 and 424) describes these structures and their secretions.

Other organs outside of the endocrine system produce hormones. The heart, for example, secretes *atrial natriuretic peptide,* a hormone that stimulates urinary sodium excretion (see chapter 17, p. 489). The kidneys secrete a red blood cell growth hormone called *erythropoietin* (see chapter 12, p. 329).

## CLINICAL APPLICATION 11.2

## Biological Rhythms

Biological rhythms are changes that systematically recur in organisms. In complex animals, they include the daily ebb and flow of biochemical levels in blood, reproductive cycles, and migration schedules. The period of any rhythm is the duration of one complete cycle. The frequency of a rhythm is the number of cycles per time unit. The study of biological rhythms is called *chronobiology*.

Three common types of rhythms in humans are ultradian, infradian, and circadian rhythms. *Ultradian rhythms* have periods shorter than 24 hours and include the cardiac cycle and the breathing cycle. Periods of *infradian rhythms,* such as the reproductive cycle, are longer than 24 hours. Periods of *circadian rhythms,* such as the sleep–wake cycle, body temperature, and hormone secretion, are approximately 24 hours.

Both external (exogenous) and internal (endogenous) factors regulate human biological rhythms. Exogenous factors are environmental components, such as daily temperature changes and the light–dark cycle. Endogenous factors include "clock" genes. Many members of an extended family in Utah, for example, have "advanced sleep phase syndrome" due to a mutation in a gene called "period." The effect is striking—they promptly fall asleep at 7:30 each night and awaken suddenly at 4:30 A.M.

The cells that respond to environmental light and dark signals are located in a part of the brain called the suprachiasmatic nuclei. Understanding how clock genes function may lead to new treatments for jet lag, insomnia, a form of advanced sleep phase syndrome that is common among older individuals, and people who work shifts longer than 12 hours.

The sleep–wake cycle is the most obvious circadian rhythm in humans. It is largely controlled by the pattern of daylight and night, but under laboratory conditions of constant light or dark, the human body eventually follows an approximately 25-hour cycle. Using a backlit electronic device, such as a smartphone or tablet, can delay falling asleep long after the device is shut off. Experiments show that such light exposure decreases melatonin production by about 22 percent.

Body temperature is mostly endogenously regulated, but light exposure and physical activity help keep this rhythm on a 24- rather than 25-hour cycle. Body temperature is usually lowest between 4 and 6 A.M., and then increases and peaks between 5 and 11 P.M. It drops during the late evening hours and into the night.

Platelet cohesion, blood pressure, and pulse rate are typically highest 2 hours after awakening. This may explain why heart attacks and strokes are more likely to occur between 6 A.M. and noon than at other times.

Plasma cortisol surges and peaks at about 6 A.M., and then gradually declines to its minimum level in late evening before increasing again in the early morning. Growth hormone secretion peaks during the night. Antidiuretic hormone secretion is greater at night, when it decreases urine formation.

## PRACTICE

42. Where is the pineal gland located?
43. What is the function of the pineal gland?
44. Where is the thymus located?
45. Which reproductive organs secrete hormones?
46. Which other organs secrete hormones?

## 11.11 | Stress and Health

Survival depends on the maintenance of homeostasis. Therefore, factors that change the body's internal environment can threaten life. When sensory receptors detect such changes, impulses to the hypothalamus trigger physiological responses that preserve homeostasis. These responses include increased activity in the sympathetic division of the autonomic nervous system and increased secretion of adrenal and other hormones. A factor that can stimulate such a response is called a *stressor,* and the condition it produces in the body is called **stress.**

### Types of Stress

Stressors include physical factors, such as exposure to extreme heat or cold, decreased oxygen concentration, infections, injuries, prolonged heavy exercise, and loud sounds. Stressors also include psychological factors, such as thoughts about real or imagined dangers, personal losses, and unpleasant social interactions. Feelings of anger, fear, grief, anxiety, depression, and guilt can also produce psychological stress. Sometimes, even pleasant stimuli, such as friendly social contact, feelings of joy and happiness, or sexual arousal, may be stressful.

### Responses to Stress

Physiological responses to stress consist of reactions called the *stress response* or *general adaptation syndrome,* which is under hypothalamic control. These reactions proceed through two stages: the immediate "alarm" stage and the long-term “resistance” stage. In the immediate response, the hypothalamus activates mechanisms that prepare the body for “fight or flight.” These mechanisms include raising blood concentrations of glucose, glycerol, and fatty acids; increasing heart rate, blood pressure, and breathing rate; dilating air passages; shunting blood from the skin and digestive organs to the skeletal muscles; and increasing epinephrine secretion from the adrenal medulla (fig. 11.18).

In the resistance response, the hypothalamus releases CRH, which stimulates the anterior pituitary to secrete ACTH, which increases cortisol secretion. Cortisol increases blood amino acid concentration, fatty acid release, and glucose formation from noncarbohydrates. Thus, while the alarm responses prepare the body for physical action to alleviate the stress, cortisol supplies cells with biochemicals required during stress (fig. 11.18).

Other hormones whose secretions increase with stress include glucagon, GH, and ADH. Glucagon and GH mobilize energy sources, such as glucose, glycerol, fatty acids, and amino acids. ADH stimulates the kidneys to retain water, which increases blood volume—particularly important if a person is bleeding or sweating heavily.

Increased cortisol secretion may be accompanied by a decrease in the number of certain white blood cells (lymphocytes), which lowers resistance to infectious diseases and some cancers. Also, excess cortisol production may raise the risk of developing high blood pressure, atherosclerosis, and gastrointestinal ulcers.

## PRACTICE

47. What is stress?
48. Distinguish between physical stress and psychological stress.
49. Describe the stress response.

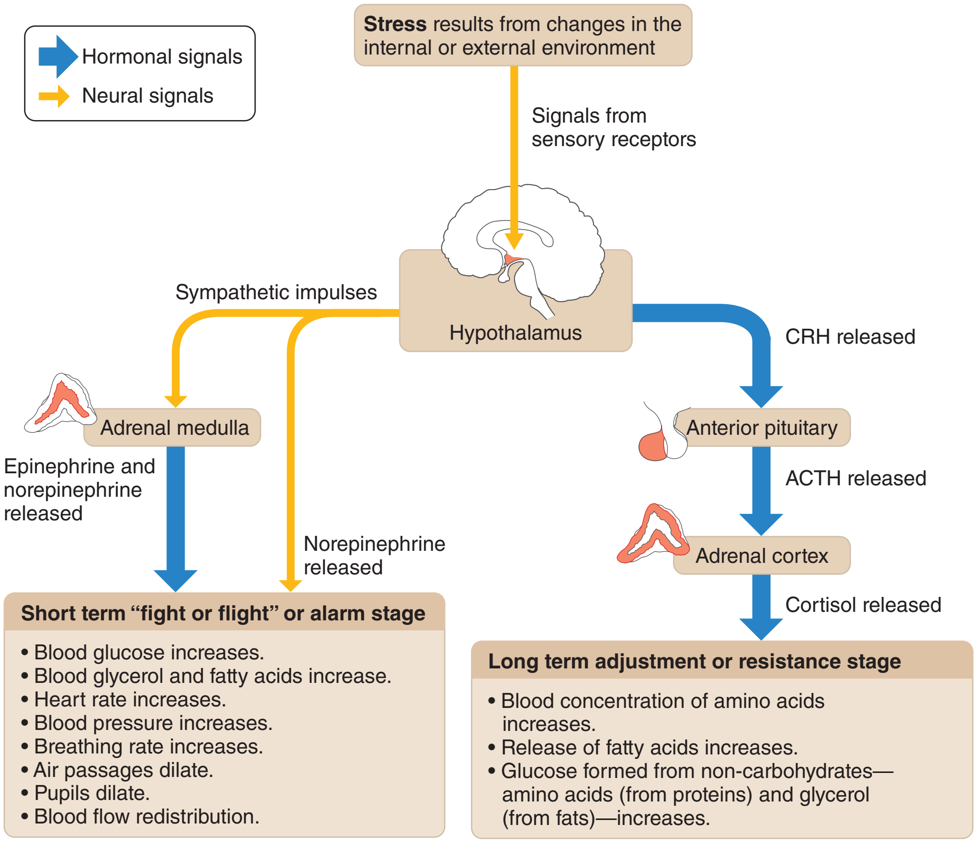
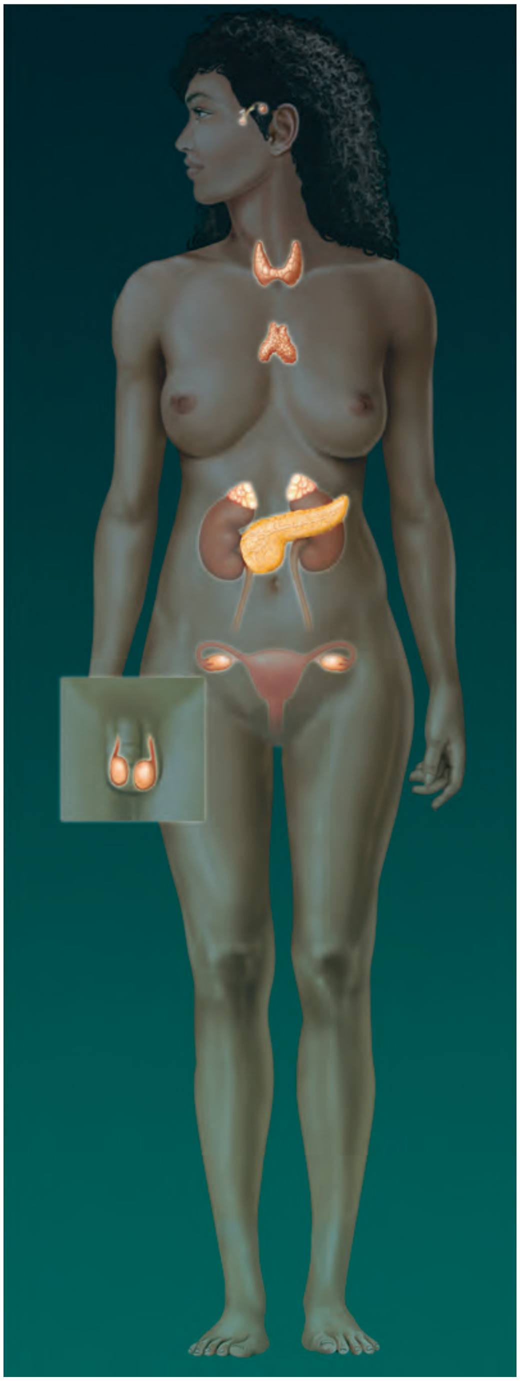

Hormonal signals
Neural signals
**Stress** results from changes in the internal or external environment
Signals from sensory receptors
Sympathetic impulses
Hypothalamus
CRH released
Adrenal medulla
Anterior pituitary
Epinephrine and norepinephrine released
ACTH released
Norepinephrine released
Adrenal cortex
Cortisol released
Short term “fight or flight” or alarm stage
• Blood glucose increases.
• Blood glycerol and fatty acids increase.
• Heart rate increases.
• Blood pressure increases.
• Breathing rate increases.
• Air passages dilate.
• Pupils dilate.
• Blood flow redistribution.
Long term adjustment or resistance stage
• Blood concentration of amino acids increases.
• Release of fatty acids increases.
• Glucose formed from non-carbohydrates—amino acids (from proteins) and glycerol (from fats)—increases.

**FIGURE 11.18** Stress response. During stress, the hypothalamus helps prepare the body for “fight or flight” by triggering sympathetic impulses to various organs. It also stimulates epinephrine release, intensifying the sympathetic responses. The hypothalamus additionally secretes corticotropin-releasing hormone, which sets into motion more lasting responses to stress.

# Endocrine System



Glands secrete hormones that have a variety of effects on cells, tissues, organs, and organ systems.

## Integumentary System

Melanocytes produce skin pigment in response to hormonal stimulation.

## Lymphatic System

Hormones stimulate lymphocyte production.

## Skeletal System

Hormones act on bones to control calcium balance.

## Digestive System

Hormones help control digestive system activity.

## Muscular System

Hormones help increase blood flow to exercising muscles.

## Respiratory System

Decreased oxygen causes hormonal stimulation of red blood cell production; red blood cells transport oxygen and carbon dioxide.

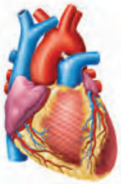
## Nervous System

Neurons control the secretions of the anterior and posterior pituitary glands and the adrenal medulla.

## Urinary System

Hormones act on the kidneys to help control water and electrolyte balance.

## Cardiovascular System



Hormones are carried in the bloodstream; some have direct actions on the heart and blood vessels.

## Reproductive System

Sex hormones play a major role in development of secondary sex characteristics, egg, and sperm.

## Summary Outline

### 11.1 Introduction (p. 302)

*The endocrine and nervous systems maintain homeostasis.*

1. The endocrine system is a network of glands that secrete hormones, which travel in the bloodstream and affect the functioning of target cells.
2. Paracrine secretions act locally, and autocrine secretions act on the cells that produce them.
3. Exocrine glands secrete through tubes or ducts.

### 11.2 General Characteristics of the Endocrine System (p. 302)

*Like the nervous system, the endocrine system exerts precise effects in helping regulate metabolic processes.*

### 11.3 Hormone Action (p. 303)

*Endocrine glands secrete hormones that affect target cells with specific receptors. Hormones are very potent.*

1. Chemically, hormones are steroids, amines, peptides, proteins, or glycoproteins.
2. Steroid hormones
   a. Steroid hormones enter a target cell and bind receptors, forming complexes in the nucleus.
   b. These complexes activate specific genes, so that specific proteins are synthesized.
3. Nonsteroid hormones
   a. Nonsteroid hormones bind receptors in the target cell membrane.
   b. The hormone-receptor complex signals a G protein to stimulate a membrane protein, such as adenylate cyclase, to induce formation of second messenger molecules.
   c. A second messenger, such as cyclic adenosine monophosphate (cAMP), diacylglycerol (DAG), or inositol triphosphate ($IP_3$), activates protein kinases.
   d. Protein kinases activate protein substrate molecules, which in turn change a cellular process.
4. Prostaglandins
   a. Prostaglandins act on the cells of the organs that produce them.
   b. Prostaglandins are present in small amounts and have powerful hormonelike effects.

### 11.4 Control of Hormonal Secretions (p. 306)

*The concentration of each hormone in body fluids is regulated.*

1. Some endocrine glands secrete hormones in response to releasing hormones that the hypothalamus and anterior pituitary secrete.
2. Other glands secrete their hormones in response to impulses from neurons.
3. Some glands respond to levels of a substance in the bloodstream.
4. Negative feedback guides these control mechanisms.
   a. In a negative feedback system, a gland senses the concentration of a substance it regulates.
   b. When the concentration of the regulated substance reaches a certain point, it inhibits the gland.
   c. As the gland secretes less hormone, the amount of the controlled substance also decreases.
   d. Negative feedback systems maintain relatively stable hormone concentrations.

### 11.5 Pituitary Gland (p. 307)

*The pituitary gland has an anterior lobe and a posterior lobe. The hypothalamus controls most pituitary secretions.*

1. Anterior pituitary hormones
   a. The anterior pituitary secretes growth hormone (GH), prolactin (PRL), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH).
   b. Growth hormone
      (1) GH stimulates cells to enlarge and divide more frequently.
      (2) GH-releasing hormone and GH release-inhibiting hormone from the hypothalamus control GH secretion.
   c. PRL stimulates and sustains milk production.
   d. Thyroid-stimulating hormone
      (1) TSH controls secretion of hormones from the thyroid gland.
      (2) The hypothalamus secretes thyrotropin-releasing hormone (TRH), which regulates TSH secretion.
   e. Adrenocorticotropic hormone
      (1) ACTH controls secretion of hormones from the adrenal cortex.
      (2) The hypothalamus secretes corticotropin-releasing hormone (CRH), which regulates ACTH secretion.
   f. FSH and LH are gonadotropins.
2. Posterior pituitary hormones
   a. The posterior lobe of the pituitary gland consists largely of neuroglia and nerve fibers.
   b. The hypothalamus produces the hormones of the posterior pituitary.
   c. Antidiuretic hormone (ADH)
      (1) ADH reduces the volume of water the kidneys excrete.
      (2) The hypothalamus regulates ADH secretion.
   d. Oxytocin (OT)
      (1) OT contracts smooth muscle in the uterine wall.
      (2) OT also contracts myoepithelial cells that secrete and eject milk.

### 11.6 Thyroid Gland (p. 310)

*The thyroid gland in the neck consists of two lobes.*

1. Structure of the gland
   a. The thyroid gland consists of many follicles.
   b. The follicles are fluid-filled and store hormones.
2. Thyroid hormones
   a. Thyroxine and triiodothyronine increase the metabolic rate of cells, enhance protein synthesis, and stimulate lipid utilization.
   b. Calcitonin decreases blood calcium level and increases blood phosphate ion concentration.

### 11.7 Parathyroid Glands (p. 312)

*The parathyroid glands are on the posterior surface of the thyroid gland.*

1. Each parathyroid gland consists of secretory cells that are well supplied with capillaries.
2. Parathyroid hormone (PTH)
   a. PTH increases blood calcium level and decreases blood phosphate ion concentration.
   b. A negative feedback mechanism operates between the parathyroid glands and the blood.

### 11.8 Adrenal Glands (p. 314)

*The adrenal glands are located atop the kidneys.*

1. Structure of the glands
   a. Each gland consists of an adrenal medulla and an adrenal cortex.
   b. These parts are functionally distinct, and secrete different hormones.
2. Hormones of the adrenal medulla
   a. The adrenal medulla secretes epinephrine and norepinephrine, which have similar effects.
   b. Sympathetic impulses stimulate secretion of these hormones.

3. Hormones of the adrenal cortex
    a. The adrenal cortex produces several steroid hormones.
    b. Aldosterone is a mineralocorticoid that causes the kidneys to conserve sodium ions and water and to excrete potassium ions.
    c. Cortisol is a glucocorticoid that affects carbohydrate, protein, and fat metabolism.
    d. Adrenal sex hormones
        (1) These hormones are of the male type but may be converted to female hormones.
        (2) They may supplement the sex hormones the gonads produce.

### 11.9 Pancreas (p. 317)

*The pancreas secretes digestive juices as well as hormones.*

1. Structure of the gland
    a. The pancreas is attached to the small intestine.
    b. The pancreatic islets secrete glucagon and insulin.
2. Hormones of the pancreatic islets
    a. Glucagon stimulates the liver to produce glucose from glycogen and noncarbohydrates.
    b. Insulin moves glucose across some cell membranes, stimulates glucose and fat storage, and promotes protein synthesis.
    c. Nerve cells do not require insulin to obtain glucose.

### 11.10 Other Endocrine Glands (p. 320)

1. Pineal gland
    a. The pineal gland is attached to the thalamus.
    b. It secretes melatonin in response to varying light conditions.
    c. Melatonin may help regulate the female reproductive cycle by inhibiting gonadotropin secretion from the anterior pituitary.
2. Thymus
    a. The thymus lies behind the sternum and between the lungs.
    b. It secretes thymosins, which affect the production of certain lymphocytes that function in immunity.
3. Reproductive organs
    a. The testes secrete testosterone.
    b. The ovaries secrete estrogens and progesterone.
    c. The placenta secretes estrogens, progesterone, and gonadotropin.
4. Digestive glands
    Certain glands of the stomach and small intestine secrete hormones.
5. Other hormone-producing organs
    Other organs, such as the heart and the kidneys, also produce hormones.

### 11.11 Stress and Health (p. 321)

*Stress occurs when the body responds to stressors that threaten the maintenance of homeostasis. Stress responses include increased activity of the sympathetic nervous system and increased secretion of adrenal hormones.*

1. Types of stress
    a. Physical stress results from environmental factors that are harmful or potentially harmful to tissues.
    b. Psychological stress results from thoughts about real or imagined dangers.
2. Responses to stress
    a. Responses to stress maintain homeostasis.
    b. The hypothalamus controls the stress response.

## CHAPTER ASSESSMENTS

### 11.1 Introduction

**1.** Define *hormone* and *target cell.* (p. 302)
**2.** Contrast endocrine glands and exocrine glands. (p. 302)

### 11.2 General Characteristics of the Endocrine System

**3.** Compare and contrast chemical communication in the nervous and endocrine systems. (p. 302)
**4.** Explain the specificity of a hormone for its target cell. (p. 302)
**5.** Functions of hormones include which of the following? (p. 302)
    a. control rates of certain chemical reactions
    b. transport substances across cell membranes
    c. help regulate water and electrolyte balances
    d. all of the above

### 11.3 Hormone Action

**6.** List the steps of steroid hormone action. (p. 304)
**7.** List the steps in the action of most nonsteroid hormones. (p. 304)
**8.** Explain how prostaglandins are similar to hormones and how they are different. (p. 306)

### 11.4 Control of Hormonal Secretions

**9.** Draw diagrams of the three mechanisms by which hormone secretion is controlled, including negative feedback. (p. 306)

### 11.5 Pituitary Gland

**10.** Describe the location and structure of the pituitary gland. (p. 307)
**11.** Explain the two ways in which the brain controls pituitary gland activity. (p. 307)
**12.** Releasing hormones come from which one of the following? (p. 307)
    a. thyroid gland
    b. anterior pituitary gland
    c. posterior pituitary gland
    d. hypothalamus

**13.** List the hormones secreted by the anterior pituitary. (p. 307)
**14.** Match the following hormones with their actions. More than one hormone can correspond to the same function. (pp. 307–309)
    (1) growth hormone
    (2) thyroid-stimulating hormone
    (3) prolactin
    (4) adrenocorticotropic hormone
    (5) follicle-stimulating hormone
    (6) luteinizing hormone

    A. milk production
    B. cell division
    C. metabolic rate
    D. exerts action on gonads
    E. controls secretion of adrenal cortex hormones

**15.** Describe the control of growth hormone secretion. (p. 308)
**16.** Prolactin does which of the following? (p. 308)
    a. stimulates breast milk secretion
    b. stimulates breast milk production
    c. inhibits breast milk secretion
    d. inhibits breast milk production

**17.** Diagram the control of thyroid hormone secretion. (p. 309)
**18.** Describe the anatomical differences between the anterior and posterior lobes of the pituitary gland. (p. 309)
**19.** Describe the functions of the posterior pituitary hormones. (p. 309)
**20.** Under which of the following conditions would you expect an increase in antidiuretic hormone secretion? (p. 309)
    a. An individual ingests excess water.
    b. The posterior pituitary is removed from an individual because of a tumor.
    c. An individual is rescued after three days in the desert without food or water.
    d. An individual with normal kidneys is producing a large volume of urine.

### 11.6 Thyroid Gland

21. Describe the location and structure of the thyroid gland. (p. 310)
22. Match the hormones from the thyroid gland with their descriptions. (p. 310)
    (1) thyroxine
    (2) triiodothyronine
    (3) calcitonin
    A. most potent at controlling metabolism
    B. regulates blood calcium
    C. has four iodine atoms
23. List the source of control for each thyroid hormone. (p. 312)

### 11.7 Parathyroid Glands

24. Describe the location and structure of the parathyroid glands. (p. 312)
25. Explain the general function of parathyroid hormone. (p. 312)
26. Draw a diagram that shows how the secretion of parathyroid hormone is regulated. (p. 313)

### 11.8 Adrenal Glands

27. Distinguish between the adrenal medulla and the adrenal cortex. (p. 314)
28. Match the adrenal hormones with their source and actions. (pp. 314–316)
    (1) cortisol
    (2) aldosterone
    (3) epinephrine
    A. cortex; sodium retention
    B. cortex; fatty acid release
    C. medulla; fight-or-flight response
29. Draw a diagram illustrating the regulation of cortisol secretion. (p. 316)

### 11.9 Pancreas

30. Describe the location and structure of the pancreas. (p. 317)
31. List the hormones secreted by the pancreatic islets, the type of cell that secretes each, and the actions of these hormones. (pp. 317–319)
32. Draw a diagram that shows how the secretion of pancreatic hormones is regulated. (pp. 317–319)

### 11.10 Other Endocrine Glands

33. Describe the location and general function of the pineal gland. (p. 320)
34. Describe the location and general function of the thymus. (p. 320)
35. Name five additional hormone-secreting organs. (p. 320)

### 11.11 Stress and Health

36. Define *stress*. (p. 321)
37. List the similarities and differences between the short-term alarm stage of stress and the long-term resistance stage. (p. 322)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 2.2, 11.3, 11.4, 11.5, 11.6

1. When reactor 4 at the Chernobyl Nuclear Power Station in Ukraine exploded at 1:23 P.M. on April 26, 1986, a great plume of radioactive isotopes erupted into the air and spread for thousands of miles. Most of the isotopes emitted immediately following the blast were of the element iodine. Which of the glands of the endocrine system would be most seriously—and immediately—affected by the blast, and how do you think this would become evident in the nearby population?

### OUTCOMES 7.3, 11.4, 11.5

2. Growth hormone is administered to people who have pituitary dwarfism. Parents wanting their normal children to be taller have requested the treatment for them. Do you think this is a wise request? Why or why not?

### OUTCOMES 11.4, 11.5

3. What hormone supplements would an adult whose anterior pituitary has been removed require?

### OUTCOMES 11.4, 11.5, 11.6, 11.11

4. How might a patient with hyperthyroidism modify lifestyle to minimize the drain on body energy resources?

### OUTCOMES 11.4, 11.8

5. The adrenal cortex of a patient who has lost a large volume of blood will increase secretion of aldosterone. What effect will this increased secretion have on the patient's blood concentrations of sodium and potassium ions?

### OUTCOMES 11.4, 11.9

6. Why might oversecretion of insulin actually reduce glucose uptake by nerve cells?

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# 12

# Blood

*Health-care workers wear personal protective equipment to shield themselves from body fluids containing disease-causing viruses.*

Universal precautions. Blood can contain more than cells, nutrients, proteins, and water—a single drop from an infected individual can harbor billions of viruses. In the wake of the AIDS epidemic, in 1988 the U.S. Centers for Disease Control and Prevention (CDC) devised "universal precautions," which are specific measures that health-care workers should take to prevent transmission of bloodborne infectious agents in the workplace. The CDC singled out HIV and the hepatitis B virus. The guidelines grew out of earlier suggestions for handling patients suspected to have been exposed to viruses. The term *universal* refers to the assumption that *any* patient may have been exposed to a pathogen that can be transmitted in a body fluid.

Attention to safety in the health-care setting can prevent transmission of infectious diseases. The World Health Organization estimates that 4–7% of new infections worldwide are transmitted via unsafe injections. Specific recommendations include:

- Use of personal protective equipment, such as gloves, goggles, and masks
- Engineering controls, such as fume hoods and sharps containers
- Work-practice controls, such as handwashing before and after performing procedures

Universal precautions were designed for, and work well in, preventing transmission of viral illnesses in settings already relatively safe, such as clinics. This isn't the case for outbreaks, natural disasters, and combat zones. For example, in 2005 several pediatric nurses who aided neighbors infected with the Marburg virus in the isolated town of Uige in Angola, in southwestern Africa, died from this hemorrhagic fever along with hundreds of other people.

Headache, fever, vomiting, and diarrhea begin three to nine days after exposure to the Marburg virus. Then the person bleeds from all body openings, internally and under the skin. Plummeting blood pressure kills most infected individuals within a week, and anyone contacting their blood is in danger of infection. Infected individuals must be isolated and not touched, but the scourge spreads because many family members become infected while tending their loved ones.

In the 2005 outbreak, contaminated medical equipment contributed to the rapid and deadly spread of the infection. Untrained clinic workers reused needles, and some people reused needles and intravenous equipment in their homes. However, even universal precautions might not have contained this outbreak, because the body fluids were so copious and infectious.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 12.1 Introduction

1. Describe the general characteristics of blood, and discuss its major functions. (p. 328)
2. Distinguish among the formed elements and the liquid portion of blood. (p. 328)

### 12.2 Blood Cells

3. Explain the significance of red blood cell counts. (p. 329)
4. Summarize the control of red blood cell production. (p. 329)
5. Distinguish among the five types of white blood cells, and give the function(s) of each type. (p. 334)

Anatomy & Physiology REVEALED apr.revealed.com **Module 9** Cardiovascular System

**12.3 Blood Plasma**

6. Describe the functions of each of the major components of plasma. (p. 336)

**12.4 Hemostasis**

7. Define *hemostasis,* and explain the mechanisms that help achieve it. (p. 339)
8. Review the major steps in blood coagulation. (p. 340)

**12.5 Blood Groups and Transfusions**

9. Explain blood typing and how it is used to avoid adverse reactions following blood transfusions. (p. 343)
10. Describe how blood reactions may occur between fetal and maternal tissues. (p. 345)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**agglutin-** [to glue together] *agglutin*ation: Clumping of red blood cells.

**bil-** [bile] *bili*rubin: Pigment excreted in the bile.

**embol-** [stopper] *embol*ism: A mass lodging in and obstructing a blood vessel.

**erythr-** [red] *erythr*ocyte: Red blood cell.

**hema-** [blood] *hema*tocrit: Percentage of red blood cells in a given volume of blood.

**hemo-** [blood] *hemo*globin: Red pigment responsible for the color of blood.

**leuko-** [white] *leuko*cyte: White blood cell.

**-osis** [abnormal condition] leukocyt*osis*: Condition in which white blood cells are overproduced.

**-poie** [make, produce] erythro*poie*tin: Hormone that stimulates the production of red blood cells.

**-stasis** [halt] hemo*stasis*: Process that stops bleeding from damaged blood vessels.

**thromb-** [clot] *thromb*ocyte: Blood platelet involved in the formation of a blood clot.

## 12.1 | Introduction

Blood signifies life, and for good reason—it has many vital functions. This complex mixture of cells, cell fragments, and dissolved biochemicals transports nutrients, oxygen, wastes, and hormones; helps maintain the stability of the interstitial fluid; and distributes heat. The blood, heart, and blood vessels form the cardiovascular system and link the body's internal and external environments.

Blood is a type of connective tissue whose cells are suspended in a liquid extracellular matrix. Blood is essential in transporting substances between body cells and the external environment, thereby promoting homeostasis.

Whole blood is slightly heavier and three to four times more viscous than water. Its cells, which form mostly in red bone marrow, include red blood cells that transport gases and white blood cells that fight disease. Blood also contains cellular fragments called blood platelets that help control blood loss. Together, the cells and platelets are termed "formed elements" of the blood, in contrast to the liquid portion, which is called **plasma** (plaz′mah) (fig. 12.1).

Most blood samples are about 45% red blood cells by volume. This percentage is called the **hematocrit (HCT).** The white blood cells and platelets account for less than 1% of blood volume. The remaining blood sample, about 55%, is the plasma, a clear, straw-colored liquid. Plasma is a complex mixture of water, amino acids, proteins, carbohydrates, lipids, vitamins, hormones, electrolytes, and cellular wastes (fig. 12.2).

Blood volume varies with body size, changes in fluid and electrolyte concentrations, and the amount of adipose tissue. An average-size adult has a blood volume of about 5 liters (5.3 quarts).

**PRACTICE**

1. What are the major components of blood?
2. What factors affect blood volume?

## 12.2 | Blood Cells

### Red Blood Cells

**Red blood cells,** or **erythrocytes** (ĕ-rith′ro-sītz), are biconcave discs. This shape is an adaptation for transporting gases; it increases the surface area through which gases can diffuse (fig. 12.3). The red blood cell's shape also places the cell membrane closer to oxygen-carrying **hemoglobin** (he″mo-glo′bin) molecules in the cell.

Each red blood cell is about one-third hemoglobin by volume. This protein imparts the color of blood. When hemoglobin binds oxygen, the resulting *oxyhemoglobin* is bright red, and when oxygen is released, the resulting *deoxyhemoglobin* is darker.

Prolonged oxygen deficiency (hypoxia) causes *cyanosis,* in which the skin and mucous membranes appear bluish due to an abnormally high blood concentration of deoxyhemoglobin in the superficial blood vessels. Exposure to low temperature may also result in cyanosis by constricting superficial blood vessels. This slows blood flow, allowing removal of more oxygen than usual from the blood flowing through the vessels, increasing the amount of deoxyhemoglobin.

Red blood cells have nuclei during their early stages of development, but lose their nuclei as they mature, providing more space for hemoglobin. Because mature red blood cells lack nuclei, they cannot synthesize proteins or divide. Red blood cells produce ATP through glycolysis only and use none of the oxygen they carry because they also lack mitochondria.

### *Red Blood Cell Counts*

The number of red blood cells in a microliter ($\mu$L or mcL or 1 mm$^3$) of blood is called the *red blood cell count* (*RBCC* or *RCC*). Although this number varies from time to time even in healthy individuals, the typical range for adult males is 4,700,000 to 6,100,000 cells per microliter, and that for adult females is 4,200,000 to 5,400,000 cells per microliter.

> The absolute numbers for red blood cell, white blood cell, and platelet counts can vary depending on how they are measured and the instruments used to measure them. For this reason, different sources may present different, but very similar, ranges of normal values.

Because increasing the number of circulating red blood cells increases the blood's *oxygen-carrying capacity*, changes in this number may affect health. For this reason, red blood cell counts are routinely consulted to help diagnose and evaluate the courses of various diseases.

### PRACTICE

3. Describe a red blood cell.
4. What is the function of hemoglobin?
5. How does a red blood cell change as it matures?
6. What is the typical red blood cell count for an adult male? For an adult female?

### *Red Blood Cell Production and Its Control*

Red blood cell formation (erythropoiesis) initially occurs in the yolk sac, liver, and spleen. After birth, these cells are produced almost exclusively by tissue lining the spaces in bones, filled with red bone marrow (chapter 7, p. 149). Figure 12.4 illustrates the stages in the formation of red blood cells from **hematopoietic** (he″mat-o-poi-et′ik) **stem cells** or *hemocytoblasts.*

The average life span of a red blood cell is 120 days. Many of these cells are removed from the circulation each day, and yet the number of cells in the circulating blood remains relatively stable. This observation suggests a homeostatic control of the rate of red blood cell production.

The hormone **erythropoietin** (ĕ-rith″ro-poi′ĕ-tin) controls the rate of red blood cell formation through *negative feedback.* The kidneys, and to a lesser extent the liver, release erythropoietin in response to prolonged oxygen deficiency (fig. 12.5). At high altitudes, for example, where the amount of oxygen in the air is reduced, blood oxygen level initially decreases. This drop in blood oxygen level triggers the release of erythropoietin, which travels via the blood to the red bone marrow and stimulates red blood cell production.

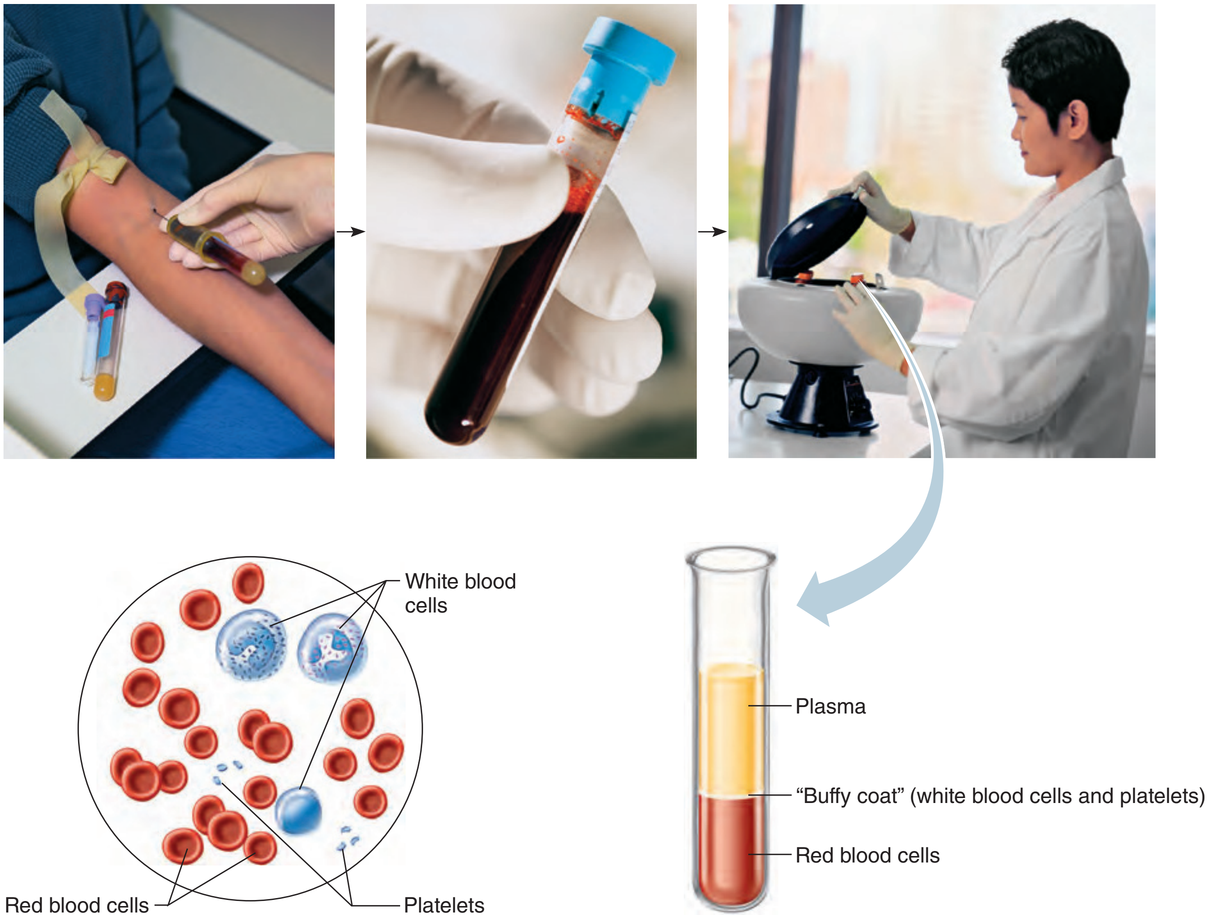
After a few days, many newly formed red blood cells appear in the circulating blood. The increased rate of production continues until the number of erythrocytes in the circulation is sufficient to supply tissues with oxygen. When the availability of oxygen returns to normal, erythropoietin release decreases, and the rate of red blood cell production returns to normal as well. An excessive increase in red blood cells is called *polycythemia.* This condition increases blood viscosity, slowing blood flow and impairing circulation.

### CAREER CORNER
## Phlebotomy Technician

The phlebotomy technician is a regular visitor to hospital inpatient rooms. Morning and night, a technician arrives with a rack of tubes for blood collection and materials to puncture veins and collect blood. The phlebotomy technician can use several blood-drawing techniques and handle other body fluids.

The phlebotomy technician explains the aseptic blood-drawing procedure, palpates arm veins to locate the best to puncture, calms common fears of needles, and prepares samples for analysis. It takes practice to remove blood as painlessly as possible!

Phlebotomy technicians work not only in hospitals but also in stand-alone blood-drawing facilities and blood donation centers, and they may travel to nursing homes and assisted living facilities. Training programs require a high school diploma. Most training programs take two to three months, and include classroom instruction (which may be done online in some programs) and practical training. All candidates for phlebotomy technician jobs must pass a national certification exam.


White blood cells
Red blood cells
Platelets
Plasma
"Buffy coat" (white blood cells and platelets)
Red blood cells

**Peripheral Blood Smear** **Centrifuged Blood Sample**

**FIGURE 12.1** APR Blood consists of a liquid portion called plasma and a solid portion (the formed elements) that includes red blood cells, white blood cells, and platelets. (Note: When blood components are separated by centrifugation, the white blood cells and platelets form a thin layer, called the "buffy coat," between the plasma and the red blood cells, which accounts for about 1% of the total blood volume.) Blood cells and platelets can be seen under a light microscope when a blood sample is smeared onto a glass slide.

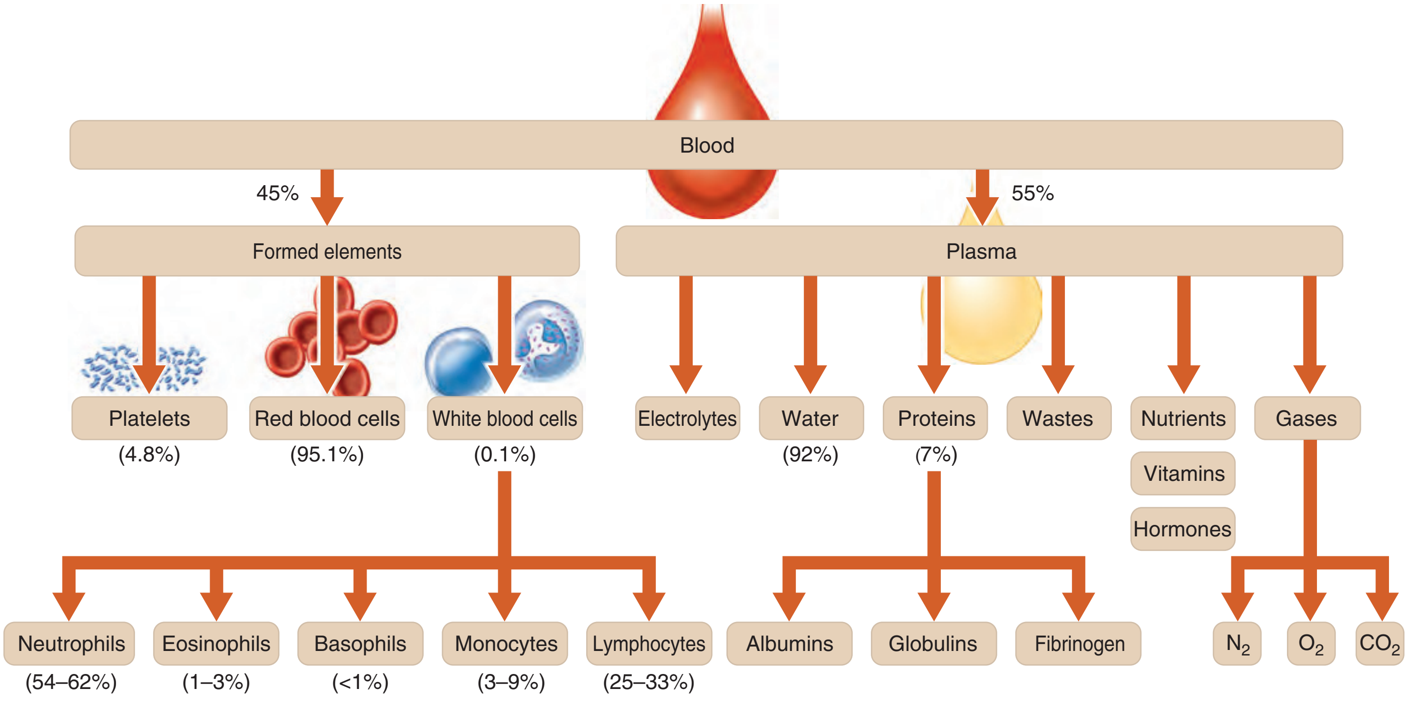

Blood
45%
55%
Formed elements
Plasma
Platelets
(4.8%)
Red blood cells
(95.1%)
White blood cells
(0.1%)
Electrolytes
Water
(92%)
Proteins
(7%)
Wastes
Nutrients
Vitamins
Hormones
Gases
Neutrophils
(54–62%)
Eosinophils
(1–3%)
Basophils
(<1%)
Monocytes
(3–9%)
Lymphocytes
(25–33%)
Albumins
Globulins
Fibrinogen
$N_2$
$O_2$
$CO_2$

**FIGURE 12.2** Blood composition. Blood is a complex mixture of formed elements in a liquid extracellular matrix, plasma.

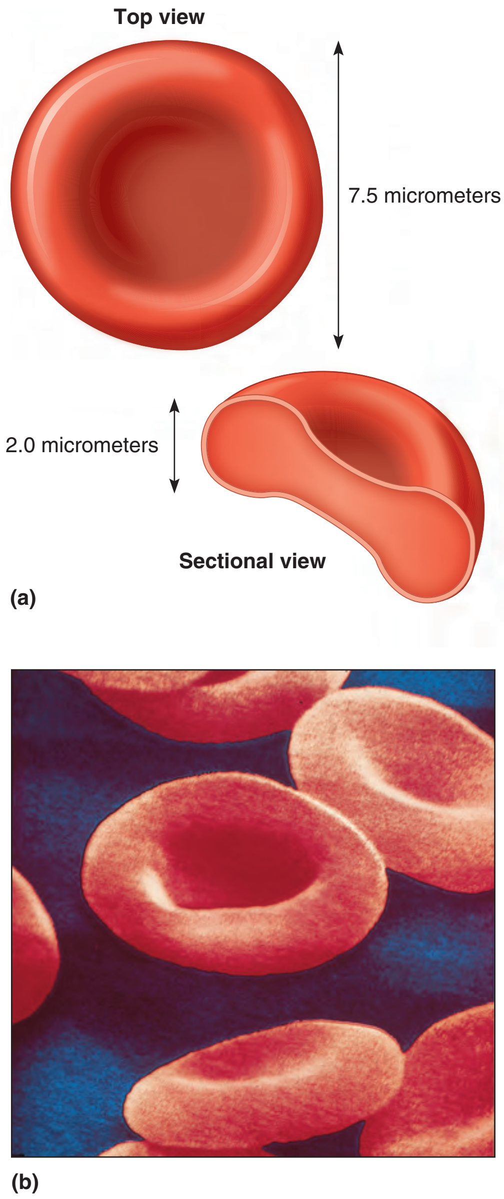


**FIGURE 12.3** APR Red blood cells. **(a)** The biconcave shape of a red blood cell makes it efficient at transporting gases. **(b)** Falsely colored scanning electron micrograph of human red blood cells (5,000×).

### *Dietary Factors Affecting Red Blood Cell Production*

Availability of B-complex vitamins—*vitamin* $B_{12}$ and *folic acid*—significantly influences red blood cell production. These vitamins are required for DNA synthesis, so they are necessary for the growth and division of cells. Cell division is rapid in blood-forming (hematopoietic) tissue, so this tissue is especially vulnerable to a deficiency of either of these vitamins. Hemoglobin synthesis and normal red blood cell production require iron. The small intestine absorbs iron slowly from food. The body reuses much of the iron released by the decomposition of hemoglobin from damaged red blood cells. Therefore, the diet need supply only small amounts of iron.

A deficiency of red blood cells or a reduction in the amount of hemoglobin they contain results in a condition called *anemia*. This reduces the oxygen-carrying capacity of the blood, and the affected person may appear pale and lack energy. A pregnant woman may become anemic if she doesn't eat iron-rich foods, because her blood volume increases due to fluid retention to accommodate the requirements of the fetus. This increased blood volume decreases the hematocrit.

In contrast to anemia, in an inherited disorder called hemochromatosis, the small intestine absorbs iron at ten times the normal rate. Iron builds up in organs, to toxic levels. Treatment is periodic blood removal, as often as every week following diagnosis. The blood is discarded.

In *sickle cell disease,* a single DNA base mutation changes one amino acid in the protein part of hemoglobin, causing hemoglobin to crystallize in a low-oxygen environment. This bends the red blood cells containing the abnormal hemoglobin into a sickle shape. The sickled cells tend to get stuck and block flow in small blood vessels, causing excruciating joint pain and damaging organs.

Children with sickle cell disease are typically diagnosed at birth. The spleen is usually damaged early on, so they receive antibiotics daily for years to prevent infection. Hospitalization for blood transfusions may be necessary for painful sickling "crises" of blocked circulation.

A drug, hydroxyurea, is used to activate production of a form of hemoglobin normally produced only in the fetus. The fetal hemoglobin slows sickling, which enables the red blood cells to reach the lungs—where fresh oxygen restores the cells' normal shapes. A bone marrow transplant or an umbilical cord stem cell transplant from a donor can completely cure sickle cell disease but have a 15% risk of fatality.

## PRACTICE

7. Where are red blood cells produced?
8. How is red blood cell production controlled?
9. Which vitamins are necessary for red blood cell production?
10. Why is iron required for the formation of red blood cells?

### *Destruction of Red Blood Cells*

Red blood cells are elastic and flexible, and they readily bend as they pass through small blood vessels. As the cells near the end of their three-month life span, however, they become more fragile and may be damaged simply passing through capillaries, particularly those in active muscles that must withstand strong contractile forces. **Macrophages** phagocytize and destroy damaged red blood cells, primarily in the liver and spleen. Recall from chapter 5, page 113, that macrophages are large, phagocytic, wandering cells.

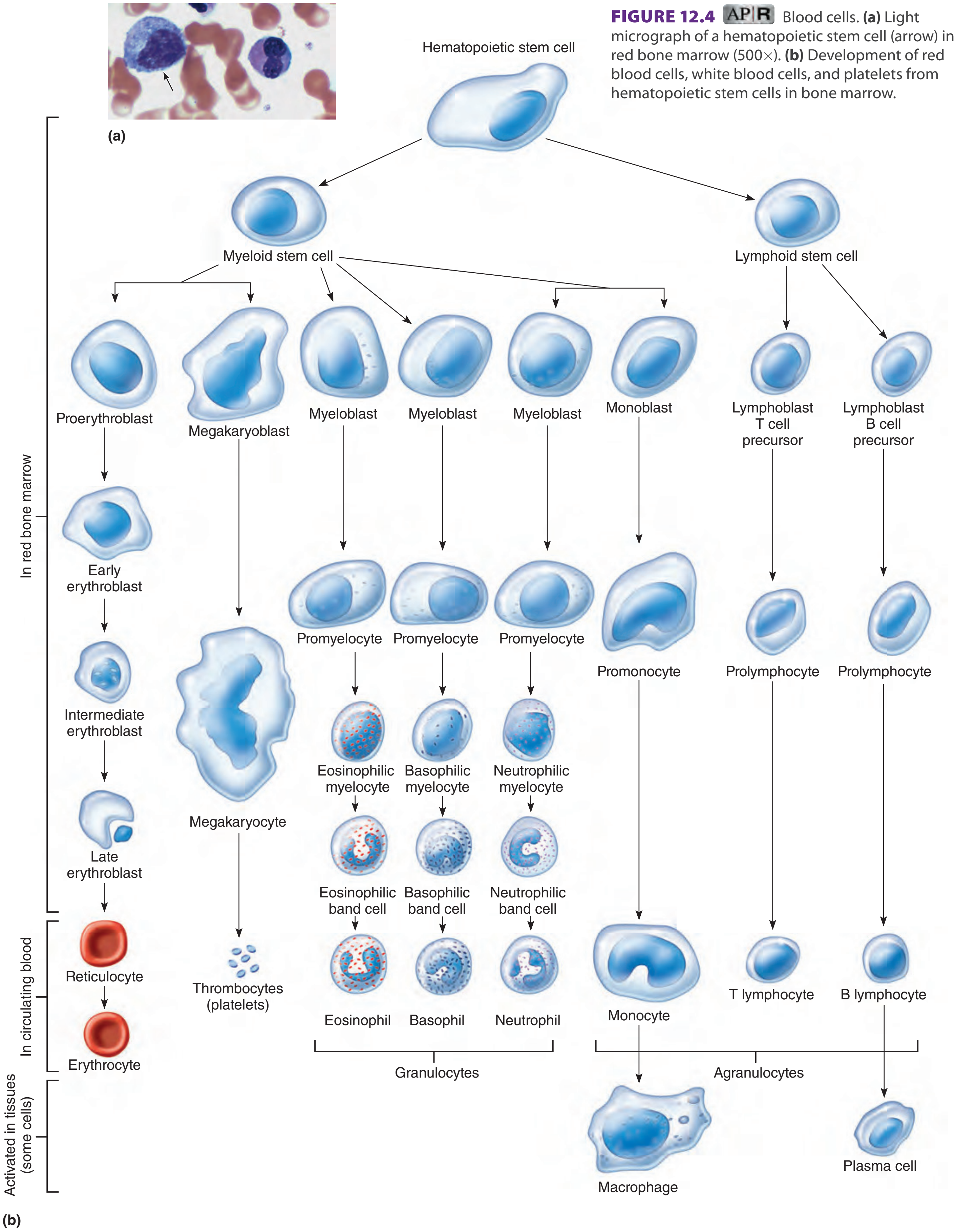

(a)
Hematopoietic stem cell
Myeloid stem cell
Lymphoid stem cell
Proerythroblast
Megakaryoblast
Myeloblast
Myeloblast
Myeloblast
Monoblast
Lymphoblast T cell precursor
Lymphoblast B cell precursor
Early erythroblast
Promyelocyte
Promyelocyte
Promyelocyte
Promonocyte
Prolymphocyte
Prolymphocyte
Intermediate erythroblast
Eosinophilic myelocyte
Basophilic myelocyte
Neutrophilic myelocyte
Late erythroblast
Megakaryocyte
Eosinophilic band cell
Basophilic band cell
Neutrophilic band cell
Reticulocyte
Thrombocytes (platelets)
Eosinophil
Basophil
Neutrophil
Monocyte
T lymphocyte
B lymphocyte
Erythrocyte
Granulocytes
Agranulocytes
Macrophage
Plasma cell
In red bone marrow
In circulating blood
Activated in tissues (some cells)
(b)

**FIGURE 12.4** APR Blood cells. **(a)** Light micrograph of a hematopoietic stem cell (arrow) in red bone marrow (500×). **(b)** Development of red blood cells, white blood cells, and platelets from hematopoietic stem cells in bone marrow.

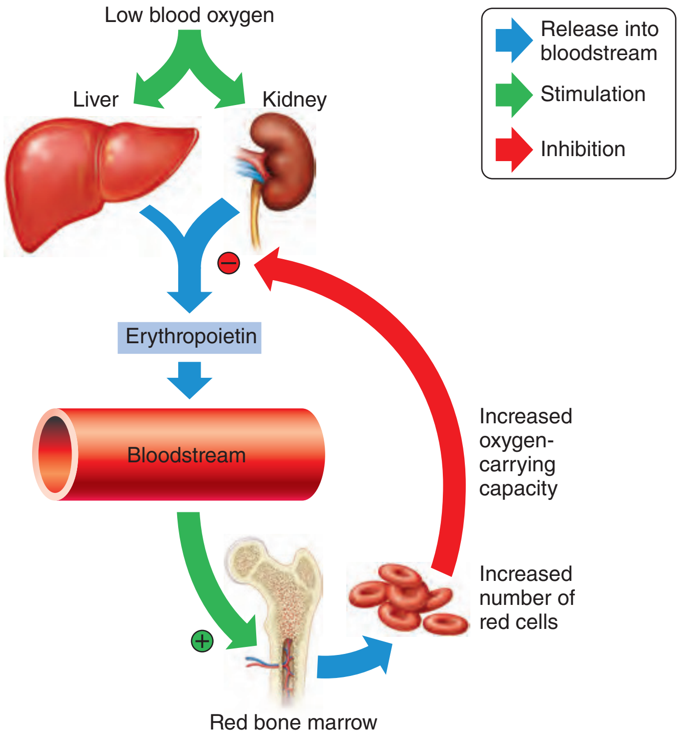
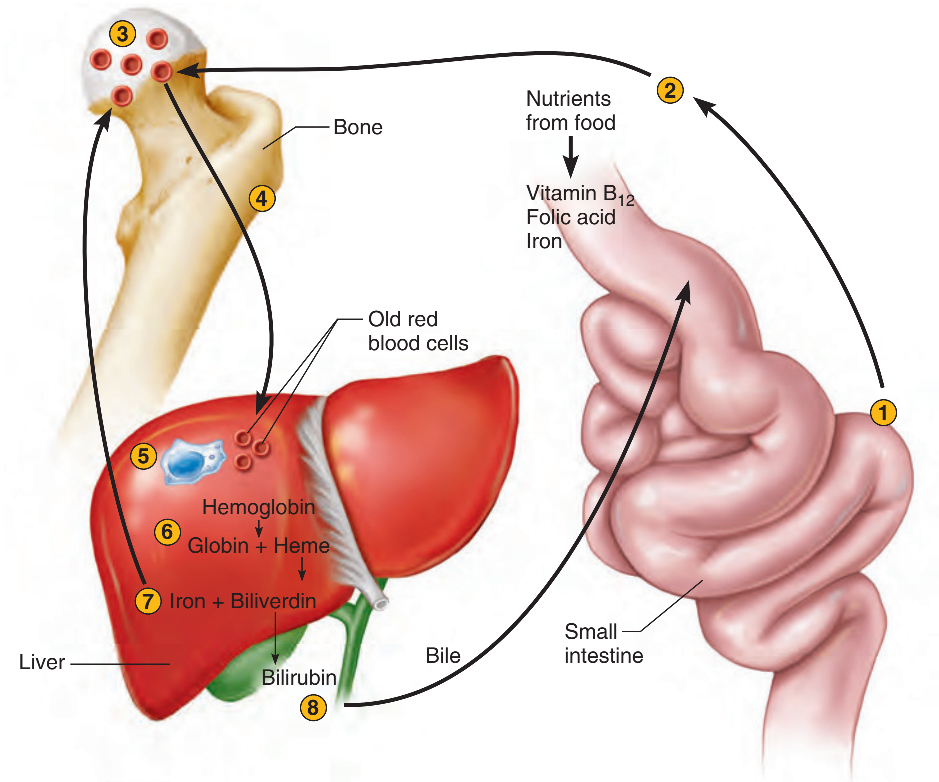

Low blood oxygen
Liver
Kidney
Erythropoietin
Bloodstream
Increased oxygen-carrying capacity
Increased number of red cells
Red bone marrow
Release into bloodstream
Stimulation
Inhibition

**FIGURE 12.5** Low blood oxygen causes the kidneys and, to a lesser degree, the liver to release erythropoietin. Erythropoietin stimulates target cells in red bone marrow to increase the production of red blood cells that carry oxygen to tissues.

Hemoglobin molecules liberated from red blood cells break down into their four component polypeptide "globin" chains, each surrounding a *heme* group. The heme further decomposes into iron and a greenish pigment called **biliverdin.** The blood may transport the iron, combined with a protein, to the hematopoietic tissue in red bone marrow to be reused in synthesizing new hemoglobin. About 80% of the iron is stored in the liver in the form of an iron-protein complex. Biliverdin eventually is converted to an orange pigment called **bilirubin.** Biliverdin and bilirubin are secreted in the bile as bile pigments (see chapter 15, p. 427). Figure 12.6 summarizes the life cycle of a red blood cell.

In jaundice (icterus), accumulation of bilirubin turns the skin and eyes yellowish. Newborns can develop *physiologic jaundice* a few days after birth.

Physiologic jaundice may be the result of immature liver cells that ineffectively secrete bilirubin into the bile. Treatment includes exposure to fluorescent light, which breaks down bilirubin in the tissues, and feedings that promote bowel movements. In hospital nurseries, babies being treated for physiologic jaundice lie under "bili lights," clad only in diapers and protective goggles. The healing effect of fluorescent light was discovered in the 1950s, when an astute nurse noted that jaundiced babies improved after sun exposure, except in the areas their diapers covered.


Bone
Nutrients from food
Vitamin $B_{12}$
Folic acid
Iron
Old red blood cells
Hemoglobin
Globin + Heme
Iron + Biliverdin
Bilirubin
Liver
Bile
Small intestine
1
2
3
4
5
6
7
8

① The small intestine absorbs nutrients.

② Blood transports absorbed nutrients.

③ Red blood cells are produced in the red bone marrow.

④ Red blood cells circulate in the bloodstream for about 120 days.

⑤ Macrophages phagocytize and break down old red cells.

⑥ Hepatocytes break down hemoglobin.

⑦ Iron is recycled via the bloodstream; biliverdin and bilirubin are secreted in the bile.

⑧ Bile is secreted into the small intestine.

**FIGURE 12.6** APR Life cycle of a red blood cell.

**PRACTICE**

11. What happens to damaged red blood cells?
12. What are the products of hemoglobin breakdown?

## White Blood Cells

**White blood cells,** or **leukocytes** (lu′ko-sītz), protect against disease. Leukocytes develop from hematopoietic stem cells in the red bone marrow (see fig. 12.4) in response to hormones, much as red blood cells form from precursors upon stimulation from erythropoietin. These hormones fall into two groups—**interleukins** and **colony-stimulating factors (CSFs).** Interleukins are numbered, while most colony-stimulating factors are named for the cell population they stimulate.

Blood transports white blood cells to sites of infection. White blood cells may then leave the bloodstream.

Normally, five types of white blood cells are in circulating blood. They differ in size, the nature of their cytoplasm, the shape of the nucleus, and their staining characteristics, and they are named for these distinctions. For example, leukocytes with granular cytoplasm are called **granulocytes,** whereas those without cytoplasmic granules are called **agranulocytes** (see fig. 12.4).

A typical granulocyte is about twice the size of a red blood cell. Members of this group include neutrophils, eosinophils, and basophils. Granulocytes develop in red bone marrow as do red blood cells, but have short life spans, averaging about 12 hours.

**Neutrophils** (nu′tro-filz) have fine cytoplasmic granules that appear light purple in neutral stain. The nucleus of an older neutrophil is lobed and consists of two to five sections (segments, so these cells are sometimes called *segs*) connected by thin strands of chromatin (fig. 12.7). Younger neutrophils are also called *bands* because their nuclei are C-shaped. Neutrophils account for 54–62% of the leukocytes in a typical blood sample from an adult.

**Eosinophils** (e″o-sin′o-filz) contain coarse, uniformly sized cytoplasmic granules that appear deep red in acid stain (fig. 12.8). The nucleus usually has only two lobes (termed bilobed). Eosinophils make up 1–3% of the total number of circulating leukocytes.

**Basophils** (ba′so-filz) are similar to eosinophils in size and in the shape of their nuclei, but they have fewer, more irregularly shaped cytoplasmic granules that appear deep blue in basic stain (fig. 12.9). Basophils usually account for less than 1% of the circulating leukocytes.

The leukocytes of the agranulocyte group include monocytes and lymphocytes. Monocytes generally arise from red bone marrow. Lymphocytes are formed in the organs of the lymphatic system, as well as in the red bone marrow (see chapter 14, p. 396).

**Monocytes** (mon′o-sītz), the largest blood cells, are two to three times greater in diameter than red blood cells (fig. 12.10). Their nuclei vary in shape and are round, kidney-shaped, oval, or lobed. They usually make up 3–9% of the leukocytes in a blood sample and live for several weeks or even months.

**Lymphocytes** (lim′fo-sītz) are only slightly larger than red blood cells. A typical lymphocyte has a large, round nucleus surrounded by a thin rim of cytoplasm (fig. 12.11). These cells account for 25–33% of circulating leukocytes. Lymphocytes may live for years.

**PRACTICE**

13. Which hormones are necessary for differentiation of white blood cells from hematopoietic stem cells in the red bone marrow?
14. Distinguish between granulocytes and agranulocytes.
15. List the five types of white blood cells, and explain how they differ from one another.

### *Functions of White Blood Cells*

White blood cells protect against infection in various ways. Some leukocytes phagocytize bacterial cells in the body, and others produce proteins (*antibodies*) that destroy or disable foreign particles.

Leukocytes can squeeze between the cells that form the walls of the smallest blood vessels. This movement, called *diapedesis* (di″ah-pĕ-de′sis)*,* allows the white blood cells to leave the circulation (fig. 12.12). Once outside the blood, they move through interstitial spaces using a form of self-propulsion called *amoeboid motion.*

The most mobile and active phagocytic leukocytes are neutrophils and monocytes. Monocytes leave the bloodstream and become **macrophages** that phagocytize bacteria, dead cells, and other debris in the tissues. Neutrophils cannot ingest particles much larger than bacterial cells, but monocytes can engulf large objects. Both of these phagocytes contain many *lysosomes,* which are organelles filled with digestive enzymes that break down organic molecules in captured bacteria, nutrients, and worn-out organelles. Neutrophils and monocytes may become so engorged with digestive products and bacterial toxins that they die.

Eosinophils are only weakly phagocytic, but they are attracted to and can kill certain parasites. Eosinophils also help control inflammation and allergic reactions by removing biochemicals associated with these reactions.

Basophils migrate to damaged tissues where they release *heparin*, which inhibits blood clotting, and *histamine,* which promotes inflammation, thus increasing blood flow to injured tissues. Basophils also play major roles in certain allergic reactions.

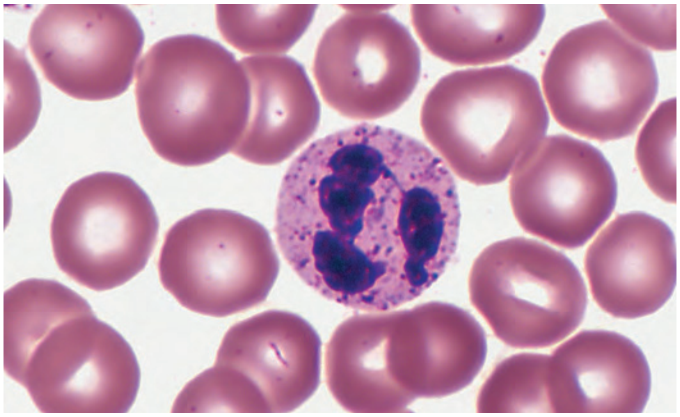


**FIGURE 12.7** APR A neutrophil has a lobed nucleus with two to five segments (2,000×).

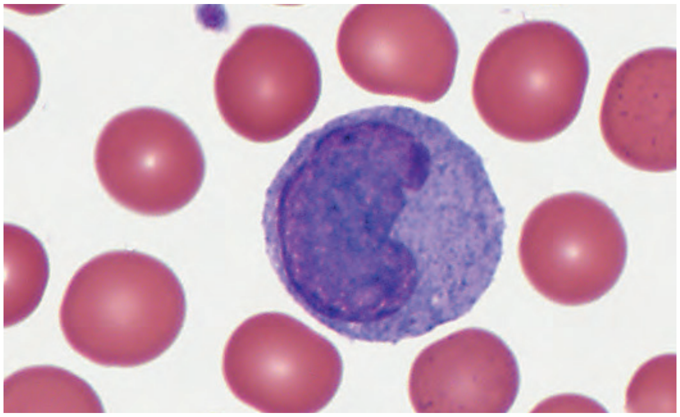


**FIGURE 12.10** APR A monocyte is the largest of the blood cells (2,000×).

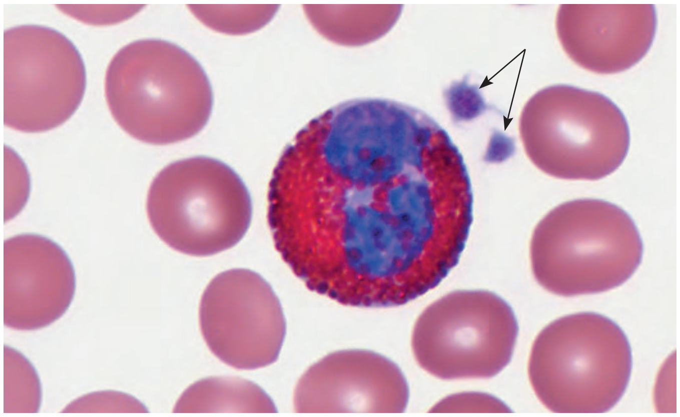


**FIGURE 12.8** APR An eosinophil has red-staining cytoplasmic granules (2,000×). Note the platelets indicated by the arrows.

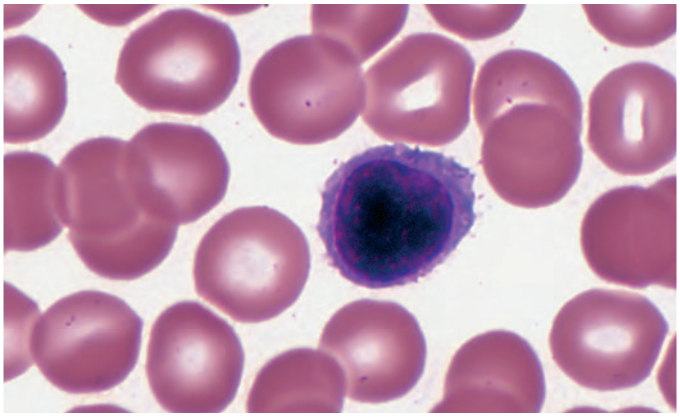


**FIGURE 12.11** APR A lymphocyte, the smallest of the white blood cells, has a large, round nucleus (2,000×).

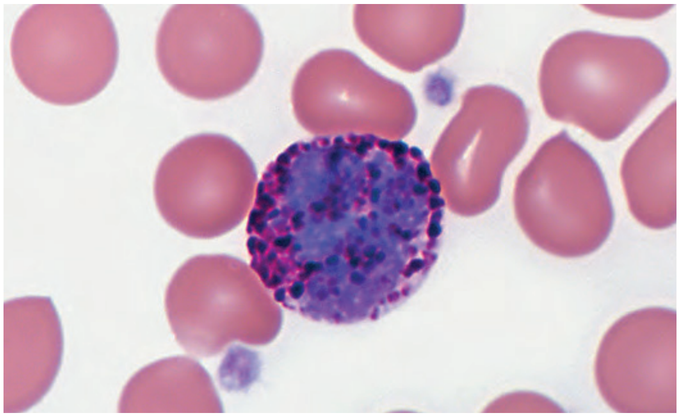


**FIGURE 12.9** APR A basophil has cytoplasmic granules that stain deep blue (2,000×).

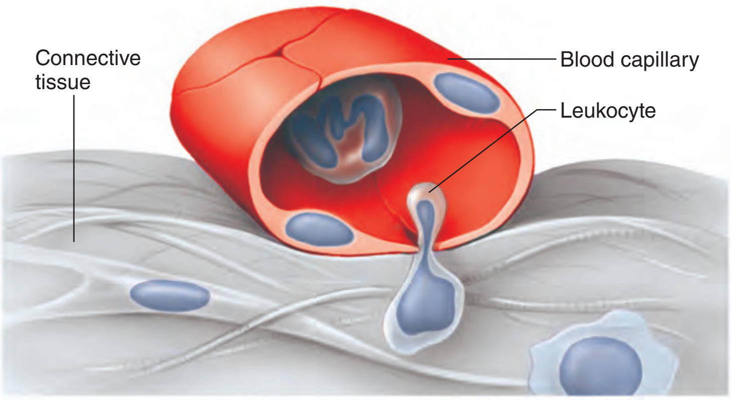


**FIGURE 12.12** In a type of movement called diapedesis, leukocytes squeeze between the endothelial cells of a capillary wall and enter the tissue space outside the blood vessel.

Q *What is a monocyte called once it has left the bloodstream and entered the tissues?*

**Answer can be found in Appendix F on page 582.**

Lymphocytes are important in *immunity.* Lymphocytes called B cells, for example, produce antibodies that attack specific foreign substances that enter the body. Chapter 14 (pp. 396–401) discusses lymphocytes and their role in immunity.

## PRACTICE

16. How do white blood cells fight infection?
17. How do white blood cells reach microorganisms that are outside blood vessels?
18. Which white blood cells are the most active phagocytes?

### *White Blood Cell Counts*

The number of white blood cells in a microliter of human blood, called the *white blood cell count* (*WBCC* or *WCC*), normally is 3,500–10,500 cells. White blood cell counts are of clinical interest because their number may change in response to abnormal conditions. A total number of white blood cells exceeding 10,500 per microliter of blood constitutes **leukocytosis,** indicating acute infection, such as appendicitis. The white blood cell count is greatly elevated in leukemia, as Clinical Application 12.1 describes.

A total white blood cell count below 3,500 per microliter of blood is called **leukopenia.** Such a deficiency may accompany typhoid fever, influenza, measles, mumps, chickenpox, AIDS, or poliomyelitis.

A *differential white blood cell count* (*DIFF*) lists percentages of the various types of leukocytes in a blood sample. This test is useful because the relative proportions of white blood cells may change in particular diseases. The number of neutrophils, for instance, usually increases during bacterial infections, and eosinophils may become more abundant during certain parasitic infections and allergic reactions. In AIDS, the number of a type of lymphocyte called a T cell drops sharply.

## PRACTICE

19. What is the normal human white blood cell count?
20. Distinguish between leukocytosis and leukopenia.
21. What is a differential white blood cell count?

### Blood Platelets AP|R

**Platelets** (plāt′letz), or **thrombocytes** (throm′bo-sĭtz), are not complete cells (see fig. 12.8). They arise from very large cells in red bone marrow, called **megakaryocytes** (meg″ah-kar′e-o-sĭtz), that fragment, releasing small pieces—platelets—into the circulation. The megakaryocytes develop long cellular extensions that break off in small sections to form platelets in the bone marrow. Megakaryocytes, and therefore platelets, develop from hematopoietic stem cells (see fig. 12.4) in response to the hormone **thrombopoietin** (throm″bo-poi′ĕ-tin).

Each platelet lacks a nucleus and is less than half the size of a red blood cell. It is capable of amoeboid movement and may live for about ten days. In normal blood, the *platelet count* varies from 150,000 to 350,000 per microliter. Platelets help close breaks in damaged blood vessels, as section 12.4 explains on page 339. Table 12.1 summarizes the characteristics of blood cells and platelets.

## PRACTICE

22. What is the normal blood platelet count?
23. What is the function of blood platelets?

## 12.3 | Blood Plasma

Plasma is the clear, straw-colored, liquid portion of the blood in which the cells and platelets are suspended. It is approximately 92% water and contains a complex mixture of organic and inorganic biochemicals. Functions of plasma include transporting gases, vitamins, and other nutrients; helping to regulate fluid and electrolyte balance; and maintaining a favorable pH.

### Plasma Proteins

**Plasma proteins** (plaz′mah pro′tēnz) are the most abundant of the dissolved substances (solutes) in plasma. These proteins remain in the blood and interstitial fluids, and ordinarily are not used as energy sources. The three main types of plasma proteins—albumins, globulins, and fibrinogen—differ in composition and function.

**Albumins** (al-bu′minz) are the smallest plasma proteins, yet account for about 60% of them by weight. Albumins are synthesized in the liver, and because they are so plentiful, they are an important determinant of the *osmotic pressure* of the plasma.

Recall from chapter 3 (p. 74) that the presence of an impermeant solute on one side of a selectively permeable membrane creates an osmotic pressure and that water always moves toward a greater osmotic pressure. Plasma proteins are too large to pass through the capillary walls, so they are impermeant, and they create an osmotic pressure that holds water in the capillaries, despite blood pressure forcing water out of capillaries by filtration (see chapter 3, pp. 74–75). The term *colloid osmotic pressure* is used to describe this osmotic effect due to the plasma proteins.

By maintaining the colloid osmotic pressure of plasma, albumins and other plasma proteins help regulate water movement between the blood and the

## CLINICAL APPLICATION 12.1

## Leukemia

When the twenty-three-year-old had a routine physical examination, she expected reassurance that her healthy lifestyle had indeed been keeping her healthy. After all, she felt great. What she got, a few days later, was a shock. Instead of having 3,500 to 10,500 white blood cells per microliter of blood, she had more than ten times that number—and many of the cells were cancerous. She had chronic myeloid leukemia (CML). Her red bone marrow was flooding her circulation with too many granulocytes, most of them poorly differentiated (figure 12A).

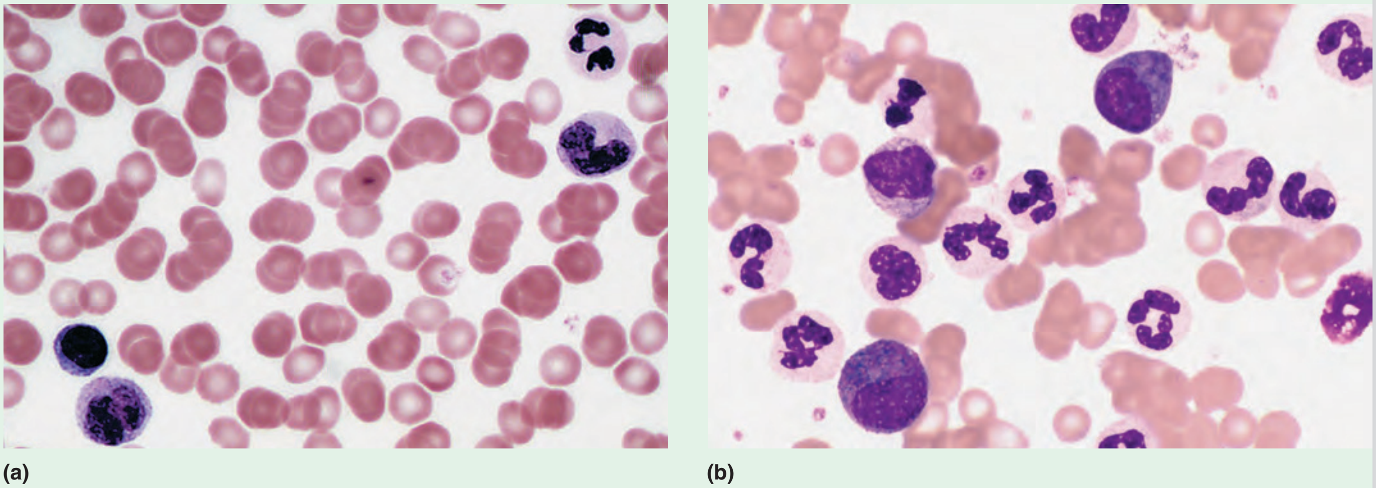
Another type of leukemia is lymphoid, in which the cancer cells are lymphocytes, produced in lymph nodes. Both myeloid and lymphoid leukemia can cause fatigue, headaches, nosebleeds and other bleeding, frequent respiratory infections, fever, bone pain, bruising, and other signs of slow blood clotting.

The symptoms arise from the disrupted proportions of the blood's formed elements and their malfunction. Immature white blood cells increase the risk of infection. Leukemic cells crowd out red blood cells and their precursors in the red marrow, causing anemia and the resulting fatigue. Platelet deficiency (thrombocytopenia) slows clotting time, causing bruises and bleeding.

Leukemia is also classified as acute or chronic. An acute condition appears suddenly, symptoms progress rapidly, and without treatment, death occurs in a few months. Chronic forms begin more slowly and may remain undetected for months or even years or, in rare cases, decades. Without treatment, life expectancy after symptoms develop is about three years.

Traditional cancer treatments destroy any cell that is actively dividing. A newer drug, Gleevec, specifically targets only the cancer cells by nestling into ATP-binding sites on a version of an enzyme called a tyrosine kinase that is found only in cancer cells. Inhibiting this enzyme prevents cancer cells from dividing. If cancer cells become resistant to Gleevec, even newer drugs are available that target the cancer cells in different ways. People with leukemia have other options. Bone marrow and stem cell transplants may cure the condition.

Another way that leukemia treatment is improving is refining diagnosis, based on identifying the proteins that leukemia cells produce. This information is used to predict which drugs are most likely to be effective, and which will cause intolerable side effects, in particular individuals. For example, some people with acute lymphoblastic leukemia (ALL), diagnosed on the basis of the appearance of the cancer cells in a blood smear, do not respond to standard chemotherapy. However, DNA microarray (also called DNA chip) technology revealed that the cells of most patients who do not improve produce different proteins than the cancer cells of patients who do respond to the drugs used to treat ALL. The nonresponders actually have a different form of leukemia, called mixed-lineage leukemia. These patients respond to different drugs.


(a)

(b)

**FIGURE 12A** Leukemia and blood cells. (**a**) Normal blood cells (700×). (**b**) Blood cells from a person with granulocytic leukemia, a type of myeloid leukemia (700×). Note the increased number of leukocytes.

## TABLE 12.1 Cellular Components of Blood

| Component | Description | Number Present | Function |
|---|---|---|---|
| Red blood cell (erythrocyte) | Biconcave disc without a nucleus; about one-third hemoglobin | 4,700,000–6,100,000 per microliter, male<br>4,200,000–5,400,000 per microliter, female | Transports oxygen and carbon dioxide |
| White blood cell (leukocyte) | | 3,500–10,500 per microliter | Destroys pathogenic microorganisms and parasites and removes worn cells |
| *Granulocytes* | About twice the size of red blood cells; cytoplasmic granules are present | | |
| 1. Neutrophil | Nucleus with two to five lobes; cytoplasmic granules stain light purple in neutral stain | 54–62% of white blood cells present | Phagocytizes small particles |
| 2. Eosinophil | Nucleus bilobed, cytoplasmic granules stain red in acid stain | 1–3% of white blood cells present | Kills parasites and moderates allergic reactions |
| 3. Basophil | Nucleus bilobed, cytoplasmic granules stain blue in basic stain | Less than 1% of white blood cells present | Releases heparin and histamine |
| *Agranulocytes* | Cytoplasmic granules are absent | | |
| 1. Monocyte | Two to three times larger than a red blood cell; nucleus shape varies from spherical to lobed | 3–9% of white blood cells present | Phagocytizes large particles |
| 2. Lymphocyte | Only slightly larger than a red blood cell; its nucleus nearly fills cell | 25–33% of white blood cells present | Provides immunity |
| Platelet (thrombocyte) | Cellular fragment | 150,000–350,000 per microliter | Helps control blood loss from broken vessels |

tissues. In doing so, they help control blood volume, which, in turn, directly affects blood pressure (see chapter 13, p. 370).

If the concentration of plasma proteins falls, tissues swell, a condition called *edema*. Low plasma protein may result from starvation, a protein-deficient diet, or from an impaired liver that cannot synthesize plasma proteins. As the concentration of plasma proteins drops, so does the colloid osmotic pressure, allowing water to leave the blood vessels and to accumulate in the interstitial spaces.

**Globulins** (glob′u-linz), which make up about 36% of the plasma proteins, can be further subdivided into *alpha, beta,* and *gamma globulins.* The liver synthesizes alpha and beta globulins, which have a variety of functions, including transport of lipids and fat-soluble vitamins. Lymphatic tissues produce the gamma globulins, which are a type of antibody (see chapter 14, p. 401).

**Fibrinogen** (fi-brin′o-jen), which constitutes about 4% of the plasma proteins, functions in blood coagulation, as discussed in section 12.4 on page 340. Synthesized in the liver, fibrinogen is the largest of the plasma proteins. Table 12.2 summarizes the characteristics of the plasma proteins.

## TABLE 12.2 Plasma Proteins

| Protein | Percentage of Total | Origin | Function |
|---|---|---|---|
| *Albumins* | 60% | Liver | Help maintain colloid osmotic pressure |
| *Globulin* | 36% | | |
| Alpha globulins | | Liver | Transport lipids and fat-soluble vitamins |
| Beta globulins | | Liver | Transport lipids and fat-soluble vitamins |
| Gamma globulins | | Lymphatic tissues | Constitute the antibodies of immunity |
| *Fibrinogen* | 4% | Liver | Plays a key role in blood coagulation |

**PRACTICE**

24. List three types of plasma proteins.
25. How do albumins help maintain water balance between the blood and the tissues?
26. What are the functions of the globulins?
27. What is the role of fibrinogen?

## Gases and Nutrients

The most important *blood gases* are oxygen and carbon dioxide. Plasma also contains a considerable amount of dissolved nitrogen, which ordinarily has no physiological function. Chapter 16 (pp. 472–474) discusses blood gases and their transport.

The *plasma nutrients* include amino acids, simple sugars, nucleotides, and lipids absorbed from the digestive tract. For example, plasma transports glucose from the small intestine to the liver, where it may be stored as glycogen or converted to fat. If blood glucose concentration drops below the normal range, glycogen may be broken down into glucose, as described in chapter 11 (p. 317). Plasma also carries recently absorbed amino acids to the liver, where they may be used to manufacture proteins, or deaminated and used as an energy source (see chapter 15, p. 426).

Plasma lipids include fats (triglycerides), phospholipids, and cholesterol. Because lipids are not water-soluble and plasma is almost 92% water, these lipids are carried in the plasma by joining with proteins.

## Nonprotein Nitrogenous Substances

Molecules that contain nitrogen atoms but are not proteins comprise a group called **nonprotein nitrogenous substances.** In plasma, this group includes amino acids, urea, uric acid, creatine (kre′ah-tin) and creatinine (kre-at′i-nin). Amino acids come from protein digestion and amino acid absorption. Urea and uric acid are products of protein and nucleic acid catabolism, respectively. Creatinine results from the metabolism of creatine. As discussed in chapter 8 (p. 195), creatine is present in *creatine phosphate* in muscle tissue as well as in the blood, where it stores energy in phosphate bonds.

## Plasma Electrolytes

Blood plasma contains a variety of *electrolytes* that are absorbed from the intestine or released as by-products of cellular metabolism. They include sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphate, and sulfate ions. Sodium and chloride ions are the most abundant. Bicarbonate ions are important in maintaining the osmotic pressure and pH of plasma, and like other plasma constituents, they are regulated so that their blood concentrations remain relatively stable. Chapter 18 discusses these electrolytes in connection with water and electrolyte balance.

**PRACTICE**

28. Which gases are in plasma?
29. Which nutrients are in plasma?
30. What is a nonprotein nitrogenous substance?
31. What are the sources of plasma electrolytes?

# 12.4 | Hemostasis

**Hemostasis** (he″mo-sta′sis) refers to the process that stops bleeding, which is vitally important when blood vessels are damaged. Following an injury to the blood vessels, several actions may help to limit or prevent blood loss, including blood vessel spasm, platelet plug formation, and blood coagulation.

## Blood Vessel Spasm

Cutting or breaking a small blood vessel stimulates **vasospasm**, the contraction of smooth muscle in its walls. Blood loss lessens almost immediately, and the ends of the severed vessel may close completely.

Although the reflex response may last only a few minutes, the effect of the direct stimulation usually continues for about 30 minutes. By then, a blockage called a *platelet plug* has formed, and blood is coagulating. Also, platelets release **serotonin,** which contracts smooth muscle in the blood vessel walls. This vasoconstriction further helps to reduce blood loss.

## Platelet Plug Formation

Platelets adhere to any rough surface, particularly to the collagen in connective tissue. When a blood vessel breaks, platelets adhere to the collagen underlying the endothelium lining blood vessels. Platelets also adhere to each other, forming a platelet plug in the vascular break. A plug may control blood loss from a small break, but a larger break may require a blood clot to halt bleeding. Figure 12.13 shows the steps in platelet plug formation.

**PRACTICE**

32. What is hemostasis?
33. How does a blood vessel spasm help control bleeding?
34. Describe the formation of a platelet plug.

## Blood Coagulation

**Coagulation** (ko-ag″u-la′shun), the most effective hemostatic mechanism, forms a *blood clot* in a series of reactions, each one activating the next. Blood coagulation

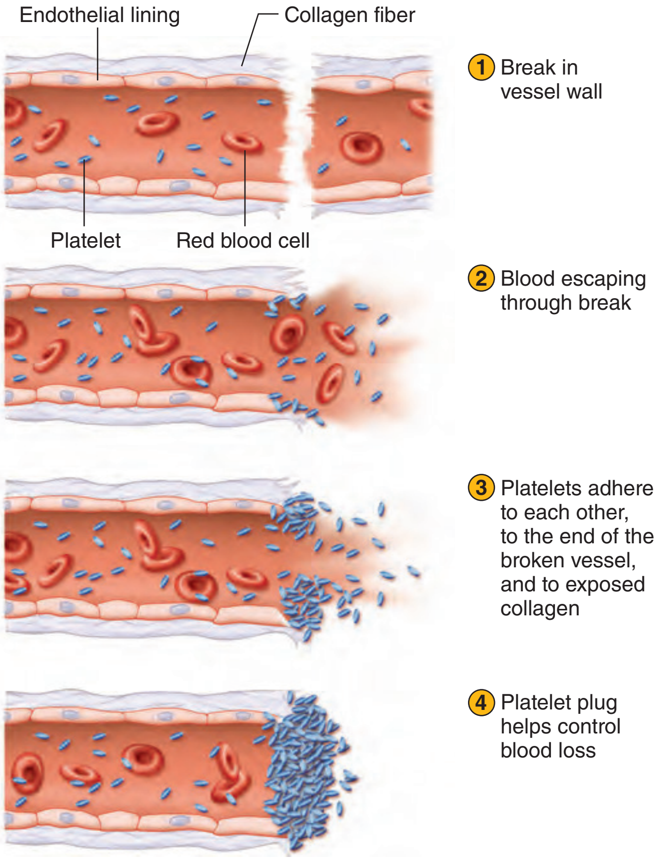

Endothelial lining
Collagen fiber
Platelet
Red blood cell
① Break in vessel wall
② Blood escaping through break
③ Platelets adhere to each other, to the end of the broken vessel, and to exposed collagen
④ Platelet plug helps control blood loss

**FIGURE 12.13** Steps in platelet plug formation.

is complex and utilizes many biochemicals called *clotting factors.* Some of these factors promote coagulation, and others inhibit it. Whether or not blood coagulates depends on the balance between these two groups of factors. Normally, anticoagulants prevail, and the blood does not clot. However, as a result of injury (trauma), biochemicals that favor coagulation may increase in concentration, and the blood may coagulate.

The major event in blood clot formation is the conversion of the soluble plasma protein fibrinogen into insoluble threads of the protein **fibrin.** Formation of fibrin takes several steps. First, damaged tissues release *tissue thromboplastin,* initiating a series of reactions that results in the production of *prothrombin activator.* This series of changes requires calcium ions as well as certain proteins and phospholipids. As its name suggests, prothrombin activator acts on prothrombin (see figure 12.16).

**Prothrombin** is an alpha globulin that the liver continually produces and is thus a normal constituent of plasma. Prothrombin activator converts prothrombin into **thrombin,** which in turn catalyzes a reaction that joins fragments of fibrinogen into long threads of fibrin.

Once fibrin threads form, they stick to the exposed surfaces of damaged blood vessels, creating a meshwork that entraps blood cells and platelets (fig. 12.14). The resulting mass is a blood clot, which may block a vascular break and prevent further blood loss. The clear, yellow liquid that remains after the clot forms is called **serum.** Serum is plasma minus the clotting factors.

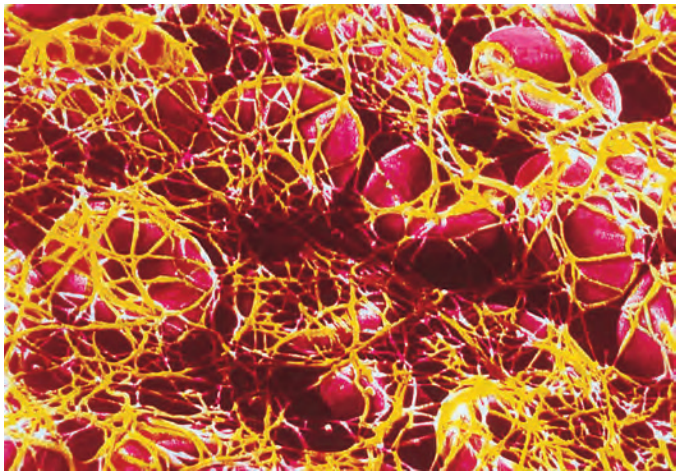


**FIGURE 12.14** Falsely-colored scanning electron micrograph of fibrin threads forming a blood clot (2,800×).

The amount of prothrombin activator in the blood is directly proportional to the degree of tissue damage. Once a blood clot begins to form, it promotes additional clotting because thrombin also acts directly on blood clotting factors other than fibrinogen, causing prothrombin to form more thrombin. This is an example of a *positive feedback system,* in which the original action stimulates more of the same type of action. Such a positive feedback mechanism produces unstable conditions and can operate for only a short time without disrupting the stable internal environment (see chapter 1, p. 16).

Laboratory tests commonly used to evaluate the blood coagulation include *prothrombin time (PT)* and *partial thromboplastin time (PTT).* These tests measure the time it takes for fibrin threads to form in a sample of plasma.

Normally, blood flow throughout the body prevents formation of a massive clot in the cardiovascular system by rapidly carrying excess thrombin away, thus keeping its concentration too low in any one place to promote further clotting. Consequently, coagulation usually occurs in blood that is standing still (or moving slowly). Clotting ceases where a clot contacts circulating blood.

Many clots, including those that form in tissues as a result of blood leakage (hematomas), disappear in time. This dissolution requires conversion of a plasma protein, *plasminogen,* to *plasmin,* a protein-splitting enzyme that can digest fibrin threads and other proteins associated with blood clots. Plasmin formation may dissolve a whole clot; however, clots that fill large blood vessels are seldom removed naturally. *Fibroblasts* (see chapter 5, p. 113) form fibrous connective tissue in the walls of the ruptured vessels to help strengthen and seal the vascular breaks.

A blood clot abnormally forming in a vessel is a **thrombus** (throm′bus). A clot that dislodges, or a fragment of a clot that breaks loose and is carried away by the blood flow, is called an **embolus** (em′bo-lus). Generally, emboli continue to move until they reach narrow places in vessels where they may lodge and block blood flow.

A blood clot forming in a vessel that supplies a vital organ, such as the heart (coronary thrombosis) or the brain (cerebral thrombosis), blocks blood flow and kills tissues the vessel serves (*infarction*) and may be fatal. A blood clot that travels and then blocks a vessel that supplies a vital organ, such as the lungs (pulmonary embolism), affects the portion of the organ the blocked blood vessel supplies. Clinical Application 12.2 discusses deep vein thrombosis.

Drugs based on "clot-busting" biochemicals can be lifesavers. *Tissue plasminogen activator* (tPA) may restore blocked cerebral circulation if given within 3 to 4 1/2 hours of a stroke. A drug derived from bacteria called *streptokinase* may also be successful, for a fraction of the cost. Another plasminogen activator used as a drug is *urokinase,* an enzyme produced by certain kidney cells. Heparin and coumadin are drugs that interfere with clot formation, but do not dissolve clots.

Abnormal clot formations are often associated with conditions that change the endothelial linings of vessels. For example, in *atherosclerosis* (ath″er-o″skle-ro′sis), accumulations of fatty deposits change arterial linings, sometimes initiating inappropriate clotting (fig. 12.15).

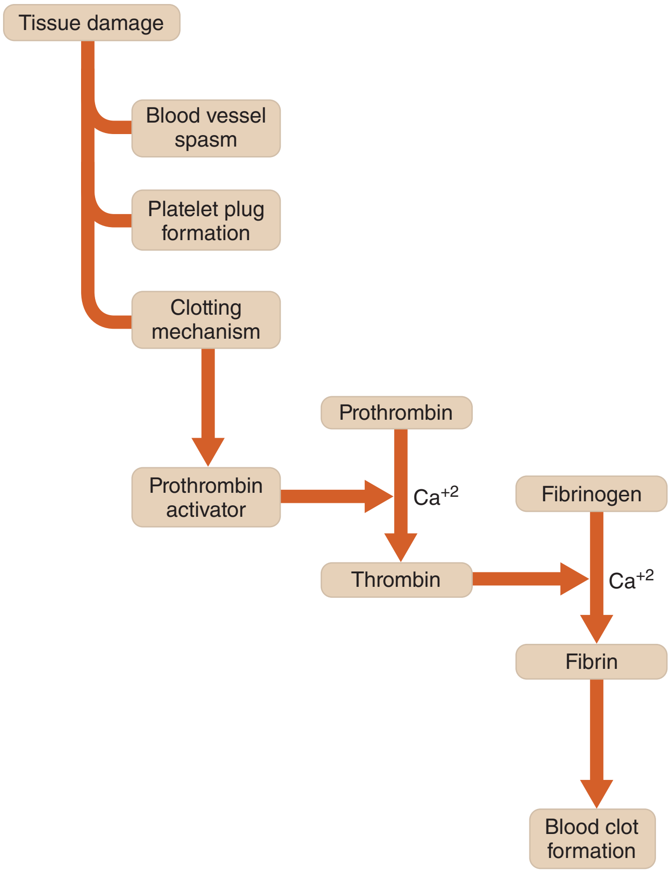


**FIGURE 12.16** The three mechanisms of hemostasis: blood vessel spasm, platelet plug formation, and blood coagulation.

**Q** *What is the major event in blood clot formation?*
**Answer can be found in Appendix F on page 582.**

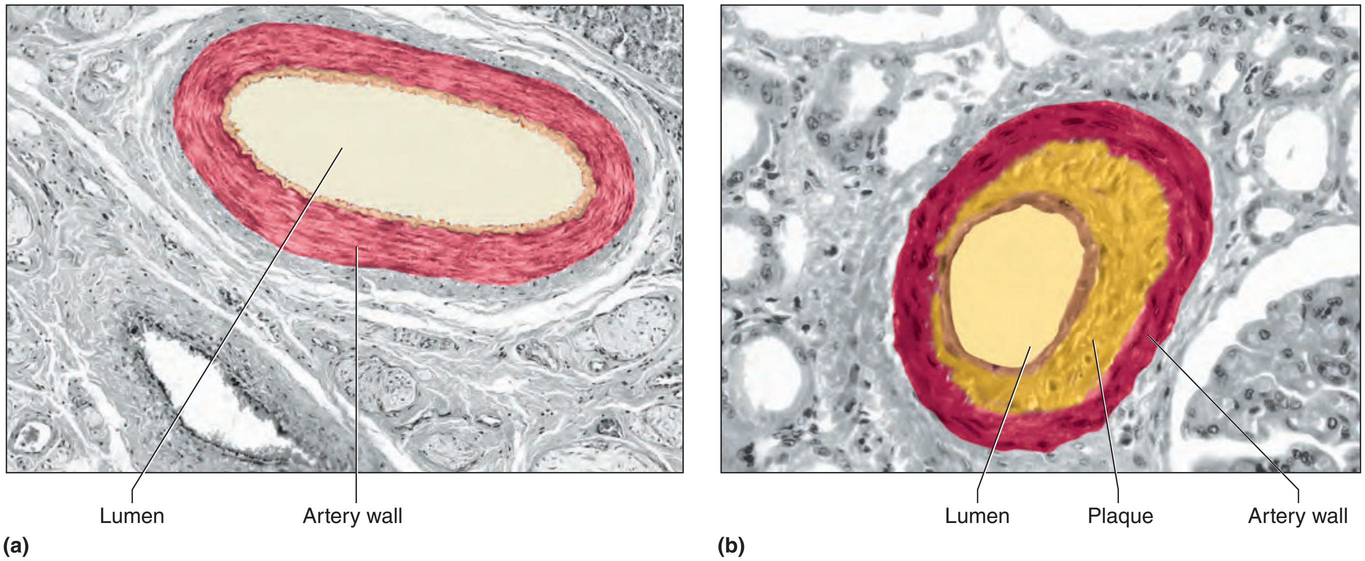


**FIGURE 12.15** Artery cross sections, falsely-colored light micrographs. **(a)** Normal artery (50×), and **(b)** the inner wall of an artery changed as a result of atherosclerosis (100×). Not only is blood flow impeded, but the uneven inner surface can snag platelets, triggering coagulation.

## CLINICAL APPLICATION 12.2

### Deep Vein Thrombosis

After a transcontinental flight, a man complained of cramps behind his knees. He mentioned the unfamiliar sensations to his traveling companion, who urged him to call his doctor. The nurse who took the call told the man to seek immediate medical attention, but because he was already starting to feel better, he didn't take her advice. Instead he continued his trip, reaching his destination after a short bus ride. Three days later, the man suddenly collapsed and died from a pulmonary embolism, a complication of the condition called deep vein thrombosis (DVT).

The man had two key risk factors for DVT: sitting for long periods, and an inherited clotting disorder that he had not known about called factor V Leiden. Other risk factors for DVT are prolonged immobility due to surgery; oral contraceptive use; hormone replacement therapy (estrogen); pregnancy; recent surgery (of the abdomen, pelvis, or limbs); and cancer (including lymphoma and cancers of the ovaries, pancreas, colon, liver, and stomach).

In DVT, stagnant blood pools, leading to clot formation, typically in the femoral or popliteal veins or in the deep veins of the pelvis. Symptoms occur in half of all affected individuals. These include deep muscle pain, redness, swelling, and possibly discoloration and dilation of surface veins (phlebitis). Part of the clot may break off hours or days after it forms and follow the path of circulation, lodging in the pulmonary arteries. This is a pulmonary embolism, and it is life-threatening. Symptoms include chest pain, anxiety, racing pulse, sweating, cough with bloody sputum, and loss of consciousness. In the United States, approximately 2 million people a year develop DVT, and 200,000 die from pulmonary embolism.

Guidelines from the American College of Chest Physicians recommend preventive measures against DVT for patients at higher risk. These actions include taking anticoagulants if immobilization is expected and wearing compression stockings that help keep blood flowing in the legs. Doing exercises while immobilized during travel is a good idea for everyone, and some airlines advise passengers on how to exercise on cramped flights, such as by curling and uncurling the toes and/or moving the feet up and down (figure 12B).

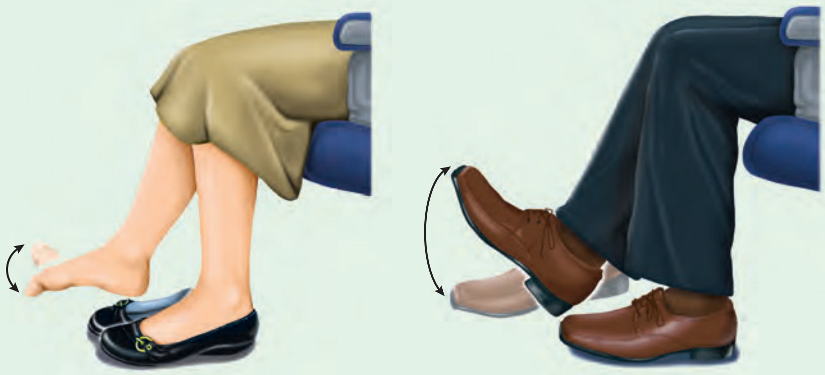


**FIGURE 12B** Exercising the toes and ankles on a long flight can lower the risk of deep vein thrombosis.

Figure 12.16 summarizes the three primary hemostatic mechanisms: blood vessel spasm, platelet plug formation, and blood coagulation.

**PRACTICE**

35. Review the major steps in blood clot formation.
36. What prevents the formation of massive clots throughout the cardiovascular system?
37. Distinguish between a thrombus and an embolus.

## 12.5 | Blood Groups and Transfusions

Early attempts to transfer blood from one person to another produced varied results. Sometimes, the recipient improved. Other times, the recipient suffered a blood transfusion reaction in which the red blood cells clumped, obstructing vessels and producing great pain and organ damage.

Eventually, scientists determined that blood is of differing types and that only certain combinations of blood types are compatible. These discoveries led to the development of procedures for typing blood. Today, safe transfusions of whole blood depend on two blood tests—"type and cross match." First the recipient's ABO blood type and Rh status (discussion below) are determined. Following this, a "cross match" is done of the recipient's serum with a small amount of the donor's red blood cells that have the same ABO type and Rh status as the recipient. Compatibility is determined by examining the mixture under a microscope for **agglutination**, the clumping of red blood cells.

## Antigens and Antibodies

An **antigen** (an′tĭ-jen), is any molecule that triggers an immune response. When the immune system encounters an antigen not found on the body's own cells it will attack, producing **antibodies** (an′tĭ-bod″ēz). In a transfusion reaction, antigens (*agglutinogens*) on the surface of the donated red blood cells react with antibodies (*agglutinins*) in the plasma of the recipient, resulting in the agglutination of the donated red blood cells.

Agglutination and coagulation are not the same! Agglutination ("clumping") is a reaction between antigens and specific antibodies. This is what happens when antigens on mismatched donated red blood cells react with antibodies in plasma. Coagulation ("clotting") is an enzymatic reaction that changes soluble fibrinogen to insoluble fibrin threads leading to the formation of a blood clot.

A mismatched blood transfusion quickly produces telltale signs of agglutination—anxiety, breathing difficulty, facial flushing, headache, and severe pain in the neck, chest, and lumbar area. Red blood cells burst, releasing free hemoglobin. Liver cells and macrophages phagocytize the hemoglobin, converting it to bilirubin, which may sufficiently accumulate to cause the yellow skin of jaundice. Free hemoglobin reaching the kidneys may ultimately cause them to fail.

Only a few of the 32 known antigens on red blood cell membranes can produce serious transfusion reactions. These include the antigens of the ABO group and those of the Rh group. Avoiding the mixture of certain kinds of antigens and antibodies prevents adverse transfusion reactions.

## ABO Blood Group

The *ABO blood group* is based on the presence (or absence) of two major antigens on red blood cell membranes—antigen A and antigen B. A and B antigens are carbohydrates attached to glycolipids projecting from the red blood cell surface. A person's erythrocytes have on their surfaces one of four antigen combinations: only A, only B, both A and B, or neither A nor B.

A person with only antigen A has *type A blood.* A person with only antigen B has *type B blood.* An individual with both antigens A and B has *type AB blood.* A person with neither antigen A nor B has *type O blood.* Thus, all people have one of four possible ABO blood types—A, B, AB, or O. The resulting ABO blood type is inherited. It is the result of DNA encoding an enzyme that catalyzes the final step in the synthesis of the A or B antigen.

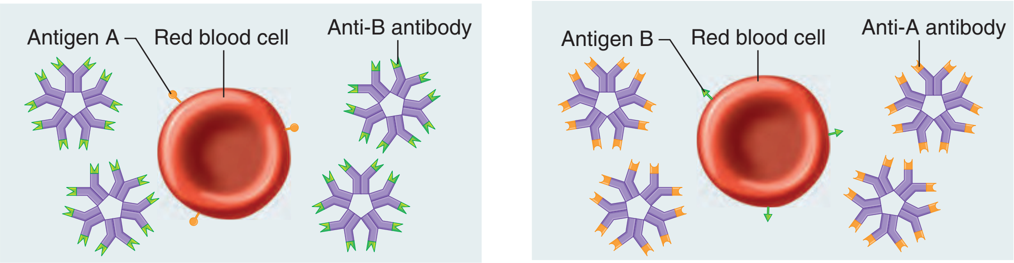
**FACTS OF LIFE** In the United States, the most common ABO blood types are O (47%) and A (41%). Rarer are type B (9%) and type AB (3%). These percentages vary in subpopulations and over time, reflecting changes in the genetic structure of populations.

Antibodies that affect the ABO blood group are synthesized in the plasma about two to eight months following birth as a result of exposure to foods or microorganisms containing the antigen(s) absent on the individual's red blood cells. Specifically, whenever antigen A is absent in red blood cells, an antibody called *anti-A* is produced, and whenever antigen B is absent, an antibody called *anti-B* is produced. Therefore, persons with type A blood have anti-B antibody in their plasma; those with type B blood have anti-A antibody; those with type AB blood have neither antibody; and those with type O blood have both anti-A and anti-B antibodies (fig. 12.17 and table 12.3). The antibodies anti-A and anti-B are large and do not cross the placenta. Thus, a pregnant woman and her fetus may be of different ABO blood types, but agglutination in the fetus will not occur.

An antibody of one type will react with an antigen of the same type and clump red blood cells (fig. 12.18); therefore, such combinations must be avoided. The major concern in blood transfusion procedures is that the cells in the donated blood not clump due to antibodies in the recipient's plasma. For this reason, a person with type A (anti-B) blood must not receive blood of type B or AB, either of which would clump in the presence of anti-B in the recipient's type A blood. Likewise, a person with type

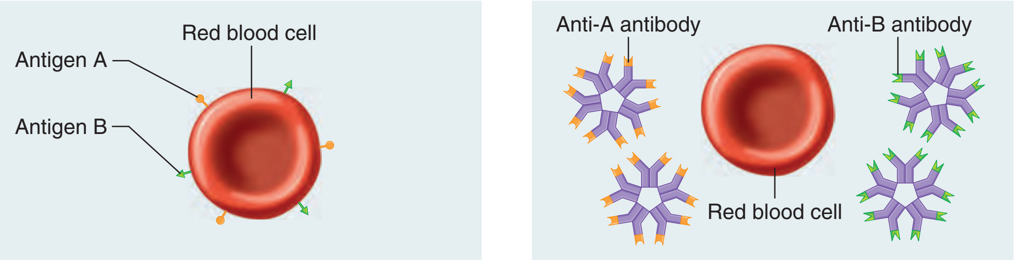
**TABLE 12.3** Antigens and Antibodies of the ABO Blood Group

| Blood Type | Antigen | Antibody |
|---|---|---|
| A | A | Anti-B |
| B | B | Anti-A |
| AB | A and B | Neither anti-A nor anti-B |
| O | Neither A nor B | Both anti-A and anti-B |



Type A blood

Type B blood



Type AB blood

Type O blood

**FIGURE 12.17** Different combinations of antigens and antibodies distinguish blood types. (Cells and antibodies not drawn to scale.)

B (anti-A) blood must not receive type A or AB blood, and a person with type O (anti-A and anti-B) blood must not receive type A, B, or AB blood.

Type AB blood lacks both anti-A and anti-B antibodies, so an AB person can receive a transfusion of blood of any other type. For this reason, type AB persons are called *universal recipients*. However, type A (anti-B) blood, type B (anti-A) blood, and type O (anti-A and anti-B) blood still contain antibodies (either anti-A and/or anti-B) that could agglutinate type AB cells if transfused rapidly. Consequently, even for AB individuals, using donor blood of the same type as the recipient is best (table 12.4).

Type O blood lacks antigens A and B. Therefore, theoretically this type could be transfused into persons with blood of any other type. Individuals with type O blood are called *universal donors*. Type O blood, however, does contain both anti-A and anti-B antibodies. If type O blood is given to a person with blood type A, B, or AB, it should be transfused slowly so that the recipient's larger blood volume will dilute the donor blood, minimizing the chance of an adverse reaction.

**TABLE 12.4** Preferred and Permissible Blood Types for Transfusions

| Blood Type of Recipient | Preferred Blood Type of Donor | If Preferred Blood Type Unavailable, Permissible Blood Type of Donor |
|---|---|---|
| A | A | O |
| B | B | O |
| AB | AB | A, B, O |
| O | O | No alternate types |

Blood in the umbilical cord at birth is rich in stem cells that can be used to treat a variety of disorders, including leukemias, sickle cell disease and other hemoglobin abnormalities, and certain inborn errors of metabolism. The United States and the United Kingdom have public umbilical cord blood banks that provide stem cells for free. For many illnesses it is more effective to receive donor stem cells, because receiving one's own could reintroduce the disease.

**PRACTICE**

38. Distinguish between antigens and antibodies.
39. What is the main concern when blood is transfused from one individual to another?
40. Why is a type AB person called a universal recipient?
41. Why is a type O person called a universal donor?

## Rh Blood Group

The *Rh blood group* was named after the rhesus monkey in which it was first studied. In humans, this group includes several Rh antigens (factors). The most prevalent of these is *antigen D*, a transmembrane protein. If the Rh antigens are present on the red blood cell membranes, the blood is said to be *Rh-positive*. Conversely, if the red blood cells lack Rh antigens, the blood is called *Rh-negative*. The presence (or absence) of Rh antigens is an inherited trait. Anti-Rh antibodies (anti-Rh) form only in Rh-negative individuals in response to the presence of red blood cells with Rh antigens. This happens, for example, if an Rh-negative person receives a transfusion of Rh-positive blood. The Rh antigens stimulate the recipient to begin producing anti-Rh antibodies. Gener-

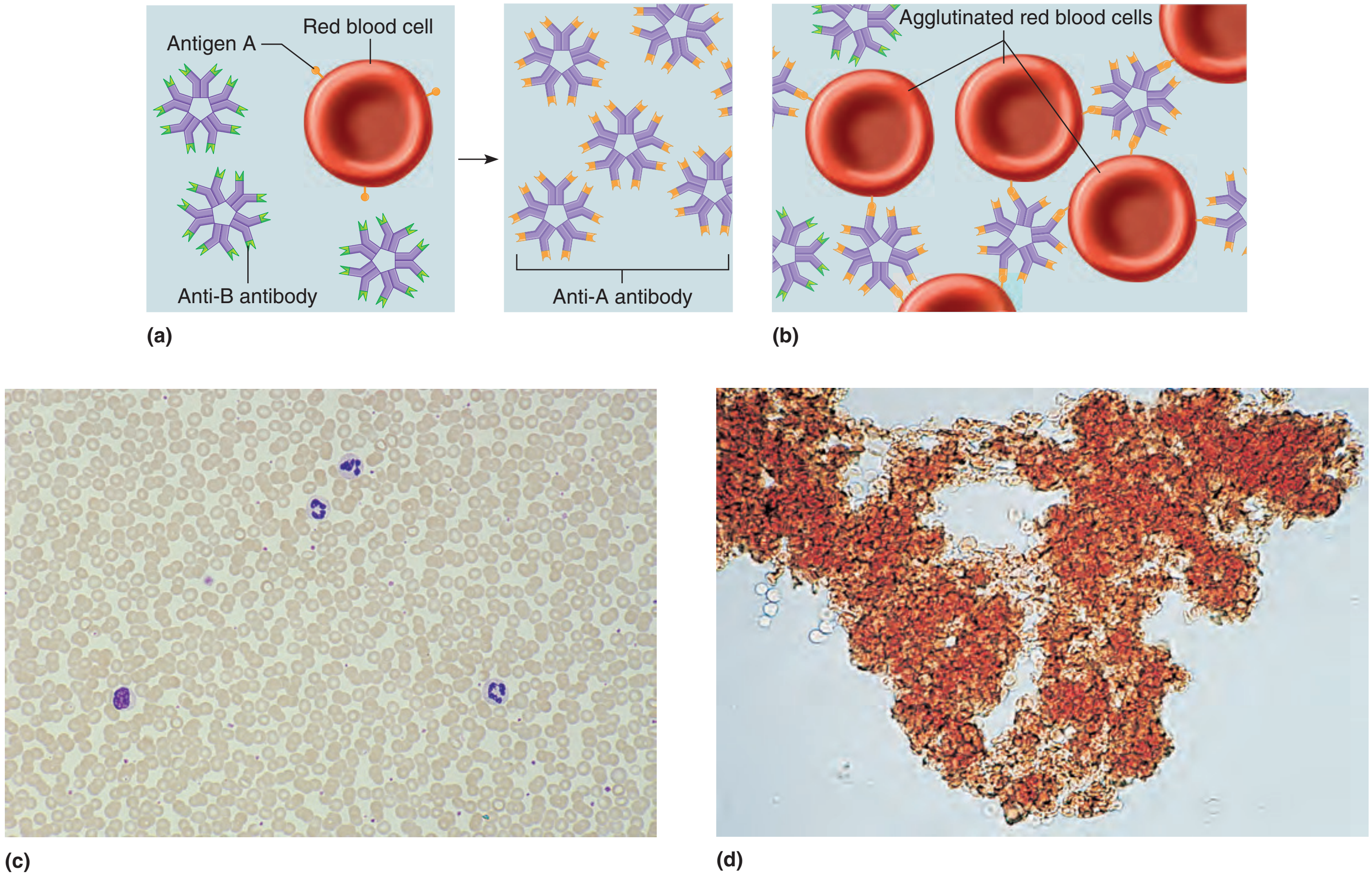


**FIGURE 12.18** Agglutination. **(a)** If red blood cells with antigen A are added to blood containing anti-A antibody, **(b)** the antibodies react with the antigens, causing clumping (agglutination). **(c)** Nonagglutinated blood (210×). **(d)** Agglutinated blood (220×). (Cells and antibodies in **(a)** and **(b)** not drawn to scale.)

ally, this initial transfusion has no serious consequences, but if the Rh-negative person—who is now sensitized to Rh-positive blood—receives another transfusion of Rh-positive blood some months later, the donated red cells are likely to agglutinate.

**FACTS OF LIFE** Only 15% of the U.S. population is Rh-negative.

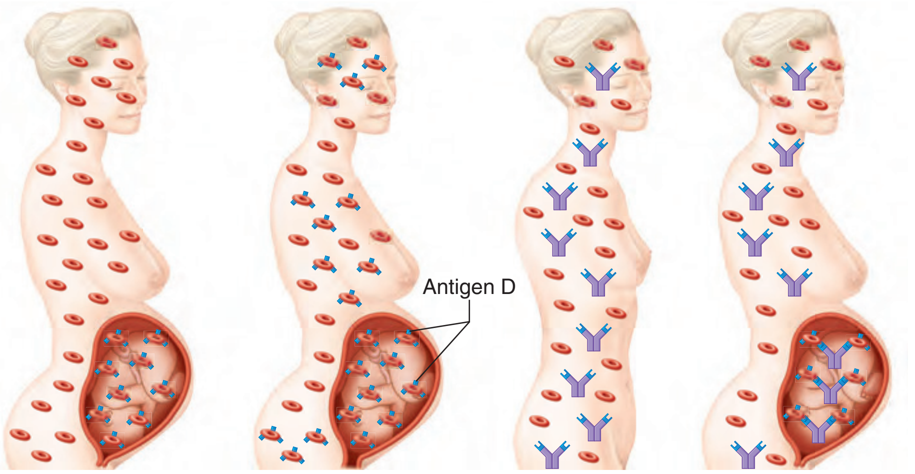
A similar situation of Rh incompatibility arises when an Rh-negative woman is pregnant with an Rh-positive fetus. Her first pregnancy with an Rh-positive fetus would probably be uneventful. However, if at the time of the infant's birth (or if a miscarriage occurs) there is tearing of the placental membranes that separated the maternal blood from the fetal blood during the pregnancy some of the infant's Rh-positive blood cells may enter the maternal circulation. These Rh-positive cells may then stimulate the maternal tissues to produce anti-Rh antibodies (fig. 12.19). If a woman who has already developed anti-Rh antibodies becomes pregnant with a second Rh-positive fetus, these antibodies, called hemolysins, cross the placental membrane and destroy the fetal red blood cells (fig. 12.19). The fetus then develops a condition called *erythroblastosis fetalis* or hemolytic disease of the fetus and newborn.

Erythroblastosis fetalis is extremely rare today because obstetricians carefully track Rh status. An Rh-negative woman who might carry an Rh-positive fetus is given an injection of a drug called RhoGAM. This injection is composed of anti-Rh antibodies, which bind to and shield any Rh-positive fetal cells that might contact the woman's cells and sensitize her immune system. RhoGAM must be given within 72 hours of possible contact with Rh-positive cells—including giving birth, terminating a pregnancy, miscarrying, or undergoing amniocentesis (a prenatal test in which a needle is inserted into the uterus).

## PRACTICE

42. What is the Rh blood group?
43. What are two ways that Rh incompatibility can arise?

**FIGURE 12.19** Rh incompatibility. If a man who is Rh-positive and a woman who is Rh-negative conceive a child who is Rh-positive, the woman's body may manufacture antibodies that attack future Rh-positive offspring.



Rh-negative female with Rh-positive fetus

During childbirth, cells from the Rh-positive fetus may enter the female's bloodstream

Female becomes sensitized—antibodies ( Y ) form against Rh-positive blood cells between pregnancies

In the next Rh-positive pregnancy, maternal antibodies attack fetal red blood cells

## Summary Outline

### 12.1 Introduction (p. 328)

*Blood is a type of connective tissue in which cells are suspended in a liquid extracellular matrix. It transports substances between body cells and the external environment, and helps maintain a stable internal environment.*

1. Blood can be separated into formed elements and liquid portions.
   a. The formed elements portion is mostly red blood cells.
   b. The liquid plasma includes water, gases, nutrients, hormones, electrolytes, and cellular wastes.
2. Blood volume varies with body size, fluid and electrolyte balance, and adipose tissue content.

### 12.2 Blood Cells (p. 328)

1. Red blood cells
   a. Red blood cells are biconcave discs with shapes that increase surface area.
   b. Red blood cells contain hemoglobin, which combines loosely with oxygen.
2. Red blood cell counts
   a. The red blood cell count equals the number of cells per microliter of blood.
   b. The average count ranges from approximately 4 to 6 million cells per microliter of blood.
   c. Red blood cell count determines the oxygen-carrying capacity of the blood. It is used to diagnose and evaluate the courses of certain diseases.
3. Red blood cell production and its control
   a. Red bone marrow produces red blood cells.
   b. In health, the number of red blood cells remains relatively stable.
   c. Erythropoietin controls the rate of red blood cell formation by negative feedback.
4. Dietary factors affecting red blood cell production
   a. Availability of vitamin $B_{12}$ and folic acid influences red blood cell production.
   b. Hemoglobin synthesis requires iron.
5. Destruction of red blood cells
   a. Macrophages in the liver and spleen phagocytize damaged red blood cells.
   b. Hemoglobin molecules decompose, and nearly all of the iron they contain is recycled.
   c. Biliverdin and bilirubin are pigments, released from the heme (iron) portion, excreted in bile.
6. White blood cells
   a. White blood cells develop from hematopoietic stem cells in red bone marrow, in response to interleukins and colony-stimulating factors.
   b. Granulocytes include neutrophils, eosinophils, and basophils.
   c. Agranulocytes include monocytes and lymphocytes.
7. Functions of white blood cells
   a. Neutrophils and monocytes phagocytize foreign particles.
   b. Eosinophils kill parasites and help control inflammation and allergic reactions.
   c. Basophils release heparin, which inhibits blood clotting, and histamine, which promotes inflammation, to increase blood flow to injured tissues.
   d. Lymphocytes are important in immunity.
8. White blood cell counts
   a. Normal total white blood cell counts vary from 3,500 to 10,500 cells per microliter of blood.
   b. The number of white blood cells may change in response to abnormal conditions, such as infections, emotional disturbances, or excessive loss of body fluids.
   c. A differential white blood cell count indicates the percentages of various types of leukocytes.
9. Blood platelets
   a. Blood platelets, which develop in the red bone marrow in response to thrombopoietin, are fragments of giant cells.
   b. The normal platelet count varies from 150,000 to 350,000 platelets per microliter of blood.
   c. Platelets help close breaks in blood vessels.

### 12.3 Blood Plasma (p. 336)

*Plasma transports gases and nutrients, helps regulate fluid and electrolyte balance, and helps maintain stable pH.*

1. Plasma proteins
    a. Plasma proteins remain in blood and interstitial fluids, and are not normally used as energy sources.
    b. Three major types exist.
        (1) Albumins help maintain the colloid osmotic pressure.
        (2) Alpha and beta globulins transport lipids and fat-soluble vitamins, and gamma globulins are the antibodies that provide immunity.
        (3) Fibrinogen functions in blood clotting.
2. Gases and nutrients
    a. Gases in plasma include oxygen, carbon dioxide, and nitrogen.
    b. Plasma nutrients include simple sugars, amino acids, and lipids.
        (1) The liver stores glucose as glycogen and releases glucose whenever blood glucose concentration falls.
        (2) Amino acids are used to synthesize proteins and are deaminated for use as energy sources.
        (3) Lipoproteins function in the transport of lipids.
3. Nonprotein nitrogenous substances
    a. Nonprotein nitrogenous substances are composed of molecules that contain nitrogen atoms but are not proteins.
    b. They include amino acids, urea, uric acid, creatine, and creatinine.
4. Plasma electrolytes
    a. Plasma electrolytes include ions of sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphate, and sulfate.
    b. Bicarbonate ions are important in maintaining the osmotic pressure and pH of plasma.

### 12.4 Hemostasis (p. 339)

*Hemostasis is the stoppage of bleeding.*

1. Blood vessel spasm
    a. Smooth muscle in blood vessel walls reflexly contract following injury.
    b. Platelets release serotonin, which stimulates vasoconstriction and helps maintain vessel spasm.
2. Platelet plug formation
    a. Platelets adhere to rough surfaces and exposed collagen.
    b. Platelets adhere to each other at injury sites and form platelet plugs in broken vessels.
3. Blood coagulation
    a. Blood clotting is the most effective means of hemostasis.
    b. Clot formation depends on the balance between factors that promote clotting and those that inhibit clotting.
    c. The basic event of coagulation is the conversion of soluble fibrinogen into insoluble fibrin.
    d. Biochemicals that promote clotting include prothrombin activator, prothrombin, and calcium ions.
    e. A thrombus is an abnormal blood clot in a vessel. An embolus is a clot or fragment of a clot that moves in a vessel.

### 12.5 Blood Groups and Transfusions (p. 342)

*Blood can be typed on the basis of cell surface antigens.*

1. Antigens and antibodies
    a. An antigen is any molecule that triggers an immune response.
    b. Antibodies are protein molecules produced in an immune response to an encounter with an antigen not found on the body's own cells.
2. ABO blood group
    a. Blood is grouped according to the presence or absence of antigens A and B attached to the surface of red blood cells.
    b. Whenever antigen A is absent, anti-A antibody is present; whenever antigen B is absent, anti-B antibody is present.
    c. Mixing red blood cells that contain an antigen with plasma that contains the corresponding antibody results in an agglutination reaction or adverse transfusion reaction in a patient.
3. Rh blood group
    a. Rh antigens are present on the red blood cell membranes of Rh-positive blood. Rh antigens are absent in Rh-negative blood.
    b. An Rh-negative person exposed to Rh-positive blood produces anti-Rh antibodies in response to the presence of Rh antigens.
    c. Mixing Rh-positive red blood cells with plasma that contains anti-Rh antibodies agglutinates the positive cells.
    d. Anti-Rh antibodies in maternal blood may cross the placental tissues and react with the red blood cells of an Rh-positive fetus.

## CHAPTER ASSESSMENTS

### 12.1 Introduction

**1.** Major functions of blood include ____________ . (p. 328)
    a. nutrient, hormone, and oxygen transport
    b. helping maintain the stability of interstitial fluid
    c. heat distribution
    d. all of the above

**2.** Formed elements in blood are ____________ , ____________ , and ____________ . (p. 328)

**3.** The liquid portion of blood is called ____________ . (p. 328)

### 12.2 Blood Cells

**4.** Describe a red blood cell. (p. 328)

**5.** Contrast oxyhemoglobin and deoxyhemoglobin. (p. 328)

**6.** Connect the significance of red blood cell counts with the function of red blood cells. (p. 329)

**7.** Describe the life cycle of a red blood cell, beginning with its production and ending with its destruction. (pp. 329–333)

**8.** List dietary factors affecting red blood cell production. (p. 331)

**9.** Name five types of leukocytes, identifying which are granulocytes and which are agranulocytes, and list the major function(s) of each type. (p. 334)

**10.** ____________ are fragments of megakaryocytes that function in ____________ . (p. 336)

### 12.3 Blood Plasma

**11.** The most abundant component of plasma is ____________ . (p. 336)
    a. waste
    b. oxygen
    c. proteins
    d. water

12. Name three types of plasma proteins, and indicate the major function(s) of each type. (p. 336)
13. Name the gases and nutrients found in plasma. (p. 339)
14. Define *nonprotein nitrogenous substances,* and name those commonly present in plasma. (p. 339)
15. The most abundant plasma electrolytes are ____________ and ____________ . (p. 339)

### 12.4 Hemostasis

16. ____________ is the term for stoppage of bleeding. (p. 339)
17. Explain how blood vessel spasm is stimulated following an injury. (p. 339)
18. Platelets adhering to form a plug may control blood loss from a ___________ break, but a larger break may require a ___________ to halt bleeding. (p. 339)
19. Describe the major steps leading to the formation of a blood clot. (p. 340)
20. Distinguish between a thrombus and an embolus. (p. 342)

### 12.5 Blood Groups and Transfusions

21. An individual with B antigens and anti-A antibodies is ABO blood type __________ . (p. 343)
22. Explain why the individual described in question 21 should not receive a transfusion with type AB blood. (p. 343)
23. Distinguish between Rh-positive and Rh-negative blood. (p. 344)
24. Describe *erythroblastosis fetalis,* and explain how this condition may develop. (p. 345)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 3.4, 12.2

1. If a patient with inoperable cancer is treated using a drug that reduces the rate of cell division, how might the patient's white blood cell count change? How might the patient's environment be modified to compensate for the effects of these changes?

### OUTCOMES 8.3, 12.2

2. Erythropoietin is available as a drug. Why would athletes abuse it?

### OUTCOME 12.2

3. How would you explain to a patient with leukemia, who has a greatly elevated white blood cell count, the importance of avoiding bacterial infections?

### OUTCOMES 12.2, 12.5

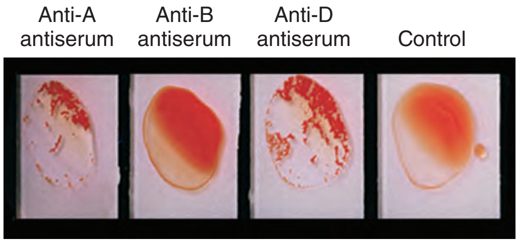
4. Why can a person receive platelets donated by anyone, but must receive a particular type of whole blood?

### OUTCOMES 12.3, 12.4

5. Why do patients with liver diseases commonly develop blood clotting disorders?

### OUTCOMES 12.5

6. Commercially available antiserum samples containing antibodies for antigens A, B, and D are used to determine the type of a particular patient's blood. The antiserum is mixed with the sample of blood, and if agglutination (clumping) occurs, that means that the antigen with the same name as the antiserum is present on those RBCs. Indicate the blood type (both ABO and Rh) of this individual. What blood type(s) could safely receive blood from this individual? What blood type(s) could this individual safely receive? (Note: The control indicates the absence of agglutination, or clumping.)



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# 13

# Cardiovascular System

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USA

*An implantable cardioverter defibrillator (ICD) delivers a shock to a heart whose ventricles are contracting wildly, restoring a normal heartbeat.*

**Cardiovascular defibrillators.** A man rushing to catch a flight at a busy airport stops suddenly, looks about in confusion, and collapses. People gather around him, as a woman runs to a device mounted on a nearby wall. It is an automated external defibrillator (AED), and looks like a laptop computer. The woman learned how to use it in a cardiopulmonary resuscitation class. She brings it over to the man, opens it, and places electrode pads over the man's chest, as indicated in a drawing on the inner cover of the defibrillator. Then the device speaks: "Analyzing heart rhythm," it declares, as a computer assesses the heart rhythm. After a short pause, the device says, "Charging, stand clear," and then "Push button." The woman does so, and the device delivers a shock to the man's chest. It assesses the heart rhythm again, and instructs the woman to deliver a second shock. Soon the man regains consciousness, just as emergency technicians arrive.

An AED in a public place can save the life of a person suffering *sudden cardiac arrest*, failure of the heart to circulate blood. One study conducted at airports found that they saved 64% of the people on whom they were used. Without defibrillation, only 5–7% of people survive sudden cardiac arrest. Each minute the odds of survival drop by 10%, and after six minutes brain damage is irreversible.

Sudden cardiac arrest can result from an abnormally accelerated heartbeat or a chaotic and irregular contraction of the heart muscle (ventricular fibrillation). The bioelectrical malfunction that usually causes these conditions may result from an artery blocked with plaque or from buildup of scar tissue from a previous myocardial infarction (heart attack).

For people who know they have an inherited disorder that causes sudden cardiac arrest (by having suffered an event and having had genetic tests), a device called an implantable cardioverter defibrillator (ICD) can be placed under the skin of the chest in a one-hour procedure. Like the AED, the ICD monitors heart rhythm. When the telltale deviations of ventricular tachycardia or ventricular fibrillation begin, it delivers a shock, preventing cardiac arrest. ICDs have been so successful in preventing cardiac arrests that they may be recommended to people at high risk for this condition.

## LEARNING OUTCOMES

***After studying this chapter, you should be able to do the following:***

### 13.1 Introduction

1. Discuss the functions of the organs of the cardiovascular system. (p. 350)

### 13.2 Structure of the Heart

2. Distinguish between the coverings of the heart and the layers that compose the wall of the heart. (pp. 350–351)
3. Identify and locate the major parts of the heart, and discuss the functions of each part. (pp. 351–353)
4. Trace the pathway of blood through the heart and the vessels of coronary circulation. (pp. 354–357)

### 13.3 Heart Actions

5. Describe the cardiac cycle and the cardiac conduction system. (pp. 357–360)
6. Identify the parts of a normal ECG pattern, and discuss the significance of this pattern. (p. 361)
7. Explain control of the cardiac cycle. (p. 362)

Anatomy & Physiology REVEALED aprevealed.com **Module 9** Cardiovascular System

LEARN PRACTICE ASSESS

### 13.4 Blood Vessels

**8.** Compare the structures and functions of the major types of blood vessels. (pp. 364–367)

**9.** Describe how substances are exchanged between blood in the capillaries and the tissue fluid surrounding body cells. (p. 367)

### 13.5 Blood Pressure

**10.** Explain how blood pressure is produced and controlled. (pp. 369–371)

**11.** Describe the mechanisms that aid in returning venous blood to the heart. (p. 372)

### 13.6 Paths of Circulation

**12.** Compare the pulmonary and systemic circuits of the cardiovascular system. (p. 373)

### 13.7–13.8 Arterial System–Venous System

**13.** Identify and locate the major arteries and veins. (pp. 373–382)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**brady-** [slow] *brady*cardia: Abnormally slow heartbeat.

**diastol-** [dilation] *diastol*ic pressure: Blood pressure when the ventricle of the heart is relaxed.

**-gram** [something written] electrocardio*gram:* Recording of the electrical changes in the myocardium during a cardiac cycle.

**papill-** [nipple] *papill*ary muscle: Small mound of muscle projecting into a ventricle of the heart.

**syn-** [together] *syn*cytium: Mass of merging cells that act together.

**systol-** [contraction] *systol*ic pressure: Blood pressure resulting from a single ventricular contraction.

**tachy-** [rapid] *tachy*cardia: Abnormally fast heartbeat.

---

## 13.1 | Introduction

At rest, the heart pumps about 7,000 liters of blood through the body each day, contracting about 2.5 billion times in an average lifetime. This muscular pump forces blood through arteries, which connect to smaller-diameter vessels called arterioles. Arterioles branch into the tiniest tubes, the capillaries, which are sites of nutrient, electrolyte, gas, and waste exchange. Capillaries converge into venules, which in turn converge into veins that return blood to the heart, completing the closed system of blood circulation. These structures—the pump and its vessels—form the **cardiovascular system.**

The cardiovascular system has two closed pathways, or circuits, of blood flow. The **pulmonary** (pul′mo-ner″e) **circuit** sends oxygen-poor blood to the lungs to pick up oxygen and unload carbon dioxide. The **systemic** (sis-tem′ik) **circuit** sends oxygen-rich blood and nutrients to all body cells and removes wastes. Without circulation, tissues would lack a supply of oxygen and nutrients, and wastes would accumulate. Such deprived cells soon begin irreversible change, which quickly leads to their death. Figure 13.1 shows the general pattern of blood transport in the cardiovascular system.

**PRACTICE**

1. Name the parts of the cardiovascular system.

## 13.2 | Structure of the Heart

The heart is a hollow, cone-shaped, muscular pump. It is in the mediastinum and rests on the diaphragm (fig. 13.2).

### Size and Location of the Heart

Heart size varies with body size. An average adult's heart is about 14 centimeters long and 9 centimeters wide (fig. 13.3).

The heart is bordered laterally by the lungs, posteriorly by the vertebral column, and anteriorly by the sternum. The *base* of the heart, which attaches to several large blood vessels, lies beneath the second rib. The heart's inferior end extends downward and to the left, terminating as a bluntly pointed *apex* at the level of the fifth intercostal space.

### Coverings of the Heart

The **pericardium** (per″ĭ-kar′de-um) is a double-layered sac that encloses the heart and the proximal ends of the large blood vessels to which it attaches. The outer layer consists of a fibrous bag, the *fibrous pericardium*, composed of dense connective tissue. It is attached to the central part of the diaphragm, the posterior of the sternum, the vertebral column, and the large blood vessels emerging from the heart.

The fibrous pericardium surrounds more delicate serous layers. The innermost layer, the *visceral pericardium* (epicardium), covers the heart. At the base of the heart, the visceral pericardium turns back upon itself to become the *parietal pericardium,* which covers the inner surface of the fibrous pericardium (figs. 13.2 and 13.4; see reference plate 3, p. 34). Between the parietal and visceral serous layers of the pericardium is a space, the *pericardial cavity,* that contains a small volume of serous fluid (fig. 13.4). This fluid reduces friction between the pericardial membranes as the heart moves within them.

> In *pericarditis,* inflammation of the pericardium is often due to viral or bacterial infection. This painful condition interferes with heart movements.

## PRACTICE

2. Where is the heart located?
3. Distinguish between the visceral pericardium and the parietal pericardium.

## Wall of the Heart

The wall of the heart is composed of three distinct layers—an outer epicardium, a middle myocardium, and an inner endocardium (fig. 13.4). The **epicardium** (ep″ĭ-kar′de-um), which corresponds to the visceral pericardium, protects the heart by reducing friction. It is a serous membrane that consists of connective tissue covered by epithelium. Its deeper portion often contains adipose tissue, particularly along the paths of coronary arteries and cardiac veins that provide blood flow through the myocardium.

The thick middle layer of the wall of the heart, or **myocardium** (mi″o-kar′de-um), consists largely of cardiac muscle tissue that pumps blood out of the heart chambers. The muscle fibers lie in planes that are separated by connective tissues richly supplied with blood capillaries, lymph capillaries, and nerve fibers.

The inner layer of the wall of the heart, or **endocardium** (en″do-kar′de-um), consists of epithelium and underlying connective tissue that contains many elastic and collagen fibers. The endocardium also contains blood vessels and some specialized cardiac muscle fibers, called *Purkinje fibers,* described in section 13.3 on page 360. The endocardium is continuous with the inner linings (endothelium) of blood vessels attached to the heart.

## Heart Chambers and Valves

Internally, the heart is divided into four hollow chambers—two on the left and two on the right (fig. 13.5). The upper chambers, called **atria** (a′tre-ah; singular, *atrium*), have thin walls and receive blood returning to the heart. Small, earlike projections called *auricles* extend anteriorly from the atria. The lower chambers, the **ventricles** (ven′trĭ-klz), receive blood from the atria and contract to force blood out of the heart into arteries.

A solid, wall-like **septum** separates the atrium and ventricle on the right side from their counterparts on the left. As a result, blood from one side of the heart never mixes with blood from the other side (except in the fetus, see chapter 20, pp. 563–564). An *atrioventricular valve* (AV valve) on the right and on the left ensures one-way blood flow between the atria and the ventricles.

The right atrium receives blood from two large veins—the *superior vena cava* and the *inferior vena cava.* A smaller vein, the *coronary sinus,* also drains venous blood into the right atrium from the myocardium.

The large **tricuspid valve,** which has three tapered projections called *cusps* as its name implies, lies between the right atrium and the right ventricle (fig. 13.5). The valve permits blood to move from the right atrium into the right ventricle and prevents backflow.

Strong, fibrous strings called **chordae tendineae** (kor′de ten′dĭ-ne) attach to the cusps of the tricuspid valve on the ventricular side. These strings originate

### CAREER CORNER

### Surgical Technician

A surgical technician enters the room of a woman scheduled to undergo heart surgery. The technician gently washes the patient. Meanwhile, another surgical technician checks that the operating room is clean, and that the surgical instruments are sterilized. She sets out the instruments on a tray in the order in which the surgeon will require them.

Surgical technicians assist doctors and nurses in gowning and gloving, and putting on masks after they've scrubbed. During the operation, surgical technicians hand instruments to the surgeon, and may prepare tissue samples, medications, and sterile dressings. An important task is to count the instruments and dressing materials before and after the procedure, to be certain none are left inside the patient. The technician may prepare the operating room for the next procedure, or accompany the patient to the recovery room. The job requires long periods of standing.

A surgical technician can specialize, such as in open heart or brain surgery. Jobs are in hospitals, dental surgical practices, and outpatient surgical facilities. Becoming a surgical technician requires an associate's (two-year) degree. Most states require certification and continuing education.

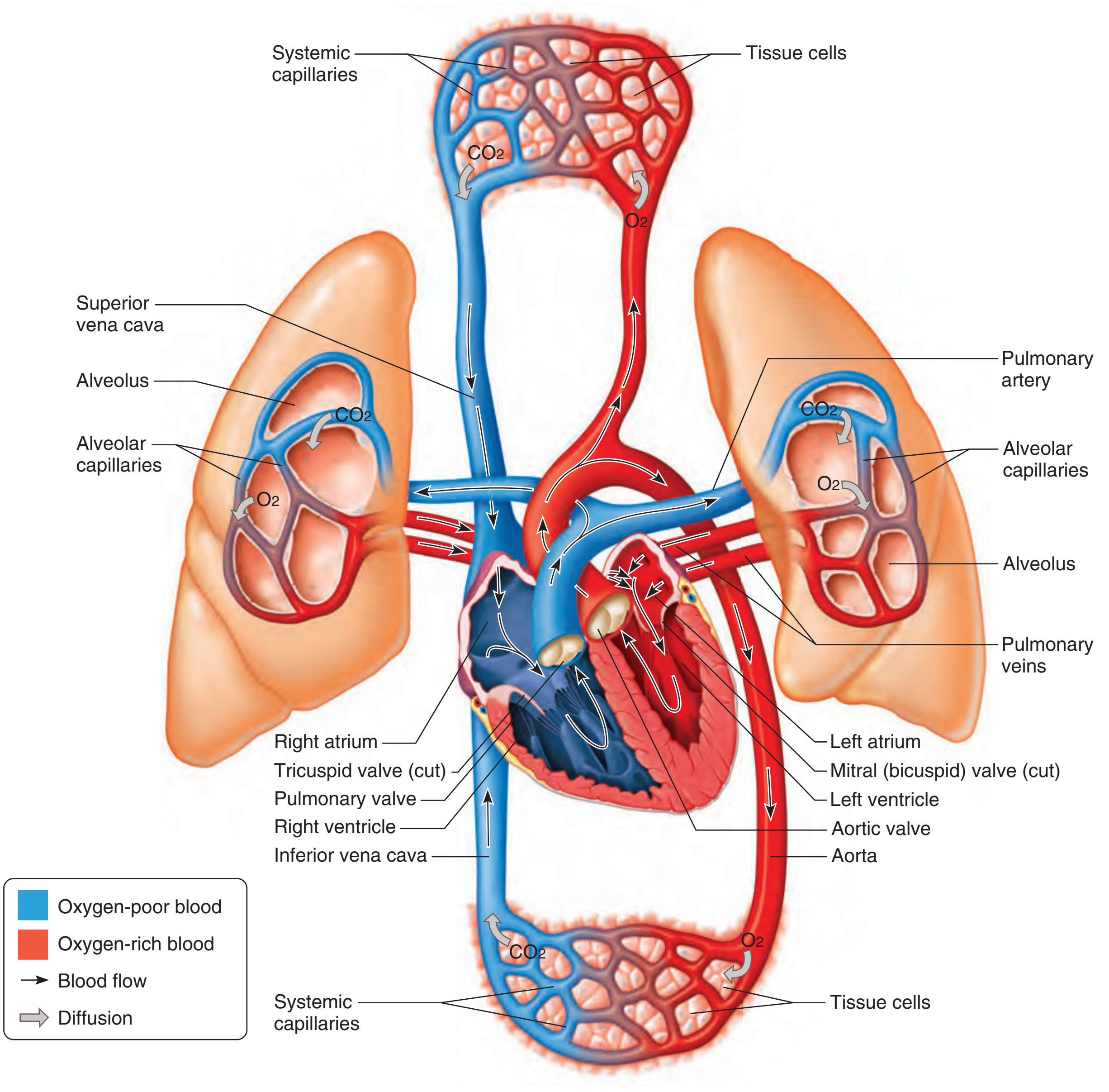

Systemic capillaries
Tissue cells
$CO_2$
$O_2$
Superior vena cava
Alveolus
$CO_2$
Alveolar capillaries
$O_2$
Pulmonary artery
$CO_2$
Alveolar capillaries
$O_2$
Alveolus
Pulmonary veins
Right atrium
Tricuspid valve (cut)
Pulmonary valve
Right ventricle
Inferior vena cava
Left atrium
Mitral (bicuspid) valve (cut)
Left ventricle
Aortic valve
Aorta
Oxygen-poor blood
Oxygen-rich blood
Blood flow
Diffusion
$CO_2$
$O_2$
Systemic capillaries
Tissue cells

**FIGURE 13.1** APR The cardiovascular system transports blood between the body cells and organs such as the lungs, intestines, and kidneys that communicate with the external environment. Vessels in the pulmonary circuit carry blood from the heart to the lungs and back to the heart, replenishing oxygen ($O_2$) and releasing the metabolic waste carbon dioxide ($CO_2$). Vessels of the systemic circuit supply all of the other cells. (Structures are not drawn to scale.)

from small mounds of cardiac muscle tissue, the **papillary muscles,** that project inward from the walls of the ventricle. The papillary muscles contract when the ventricle contracts. As the tricuspid valve closes, these muscles pull on the chordae tendineae and prevent the cusps from swinging back (everting) into the atrium.

The right ventricle has a thinner muscular wall than the left ventricle (fig. 13.5). This right chamber pumps blood a fairly short distance to the lungs against a relatively low resistance to blood flow. The left ventricle, on the other hand, must force blood to all the other parts of the body against a much greater resistance to flow.

When the muscular wall of the right ventricle contracts, the blood inside its chamber is put under increasing pressure, and the tricuspid valve closes passively. As a result, the only exit for the blood is through the *pulmonary trunk,* which divides to form the left and right *pulmonary arteries* that lead to the lungs. At the base of this trunk is a **pulmonary valve** which consists of three cusps. This valve allows blood to leave the right ventricle and prevents backflow into the ventricular chamber (fig. 13.6).

The left atrium receives blood from the lungs through four *pulmonary veins*—two from the right lung and two from the left lung. Blood passes from the left

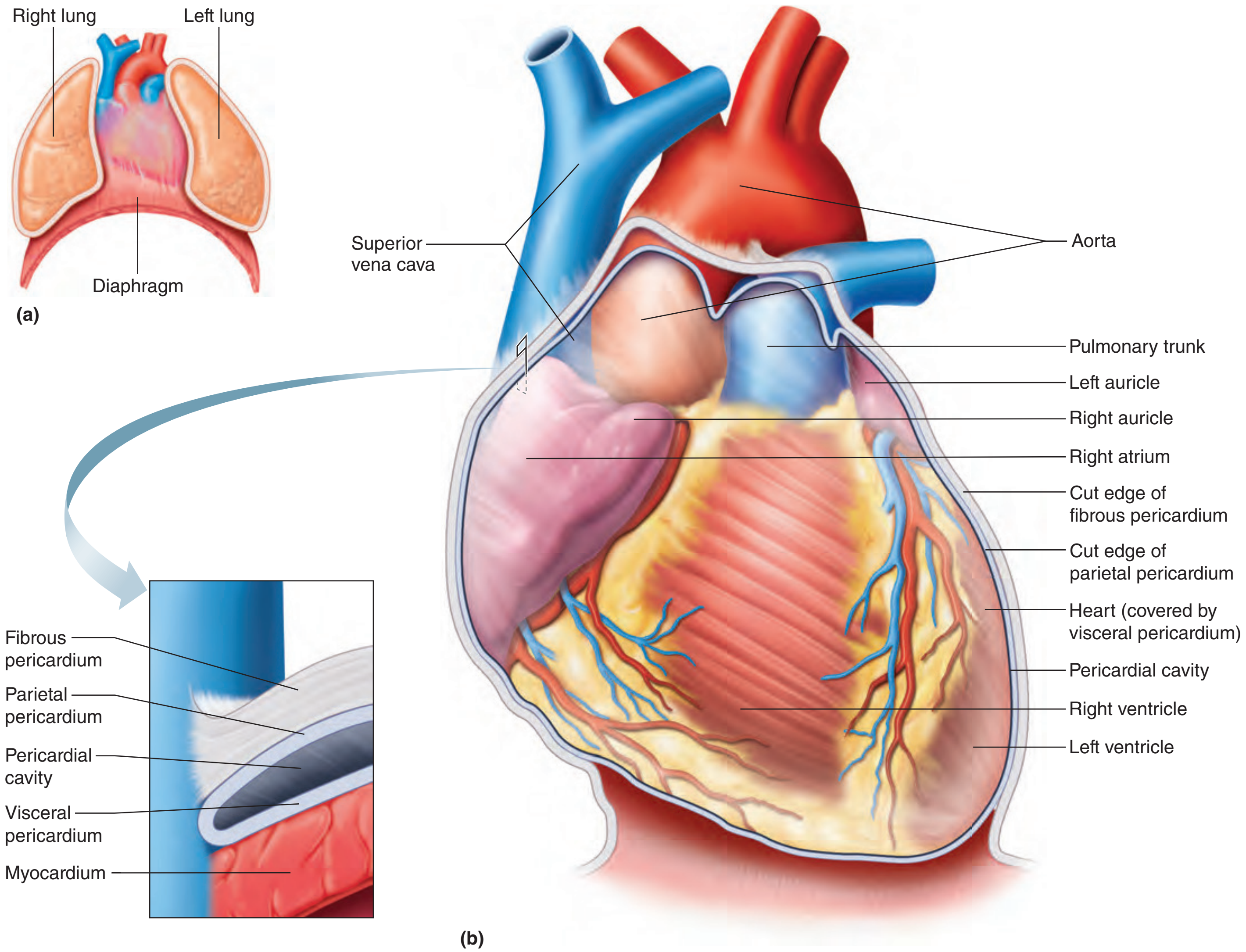

Right lung
Left lung
Diaphragm
(a)
Superior vena cava
Aorta
Pulmonary trunk
Left auricle
Right auricle
Right atrium
Cut edge of fibrous pericardium
Cut edge of parietal pericardium
Heart (covered by visceral pericardium)
Pericardial cavity
Right ventricle
Left ventricle
Fibrous pericardium
Parietal pericardium
Pericardial cavity
Visceral pericardium
Myocardium
(b)

**FIGURE 13.2** APR The heart is within the mediastinum and is enclosed by a layered pericardium.

atrium into the left ventricle through the **mitral valve** (shaped like a mitre, a type of headpiece), or bicuspid valve, which prevents blood from flowing back into the left atrium from the left ventricle (see fig. 13.5). As with the tricuspid valve, the papillary muscles and the chordae tendineae prevent the cusps of the mitral valve from swinging back into the left atrium.

When the left ventricle contracts, the mitral valve closes passively, and the only exit is through a large artery, the **aorta** (a-or′tah). At the base of the aorta is the **aortic valve** (a-or′tik valv), which consists of three cusps (fig. 13.6). The aortic valve opens and allows blood to leave the left ventricle as it contracts. When the ventricular muscles relax, this valve closes and prevents blood from backing up into the left ventricle.

The mitral and tricuspid valves are called atrioventricular valves because they are between atria and ventricles. The pulmonary and aortic valves are called "semilunar" because of the half-moon shapes of their cusps. Table 13.1 summarizes the locations and functions of the heart valves.

*Mitral valve prolapse (MVP)* affects up to 6% of the U.S. population. In this condition, one (or both) of the cusps of the mitral valve stretches and bulges into the left atrium during ventricular contraction. The valve usually continues to function adequately, but sometimes blood regurgitates (flows back) into the left atrium. Symptoms of MVP include chest pain, palpitations, fatigue, and anxiety.

People with MVP are particularly susceptible to infective endocarditis. This inflammation of the endocardium due to an infection appears as a plantlike growth on the mitral valve. Some people with MVP may be advised by their physicians to take antibiotics before undergoing dental work to prevent *Streptococcus* bacteria in the mouth from migrating through the blood to the heart and causing this infection.

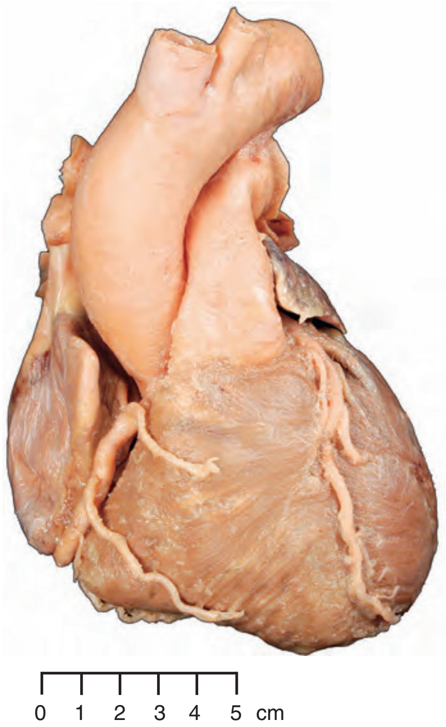


**FIGURE 13.3** Anterior view of a human heart. This photo is not life-size, so a proportionately reduced ruler has been included as a size reference to help the student grasp the true size of the organ.

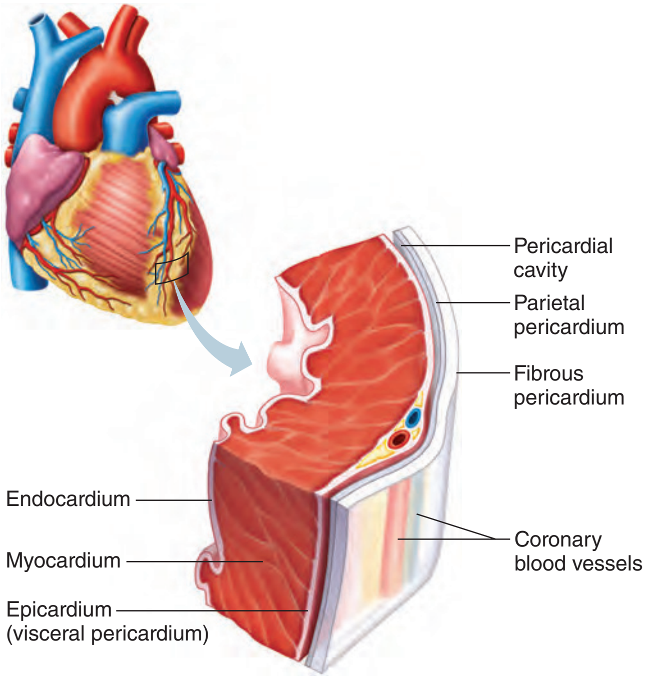


**FIGURE 13.4** APR The heart wall has three layers: an endocardium, a myocardium, and an epicardium.

**PRACTICE**

4. Describe the layers of the heart wall.
5. Name and locate the four chambers of the heart.
6. Describe the function of each heart valve.

## Skeleton of the Heart

Rings of dense connective tissue surround the pulmonary trunk and aorta at their proximal ends. These rings provide firm attachments for the heart valves and for muscle fibers; they also prevent the outlets of the atria and ventricles from dilating during contraction. The fibrous rings, together with other masses of dense connective tissue in the part of the septum between the ventricles (interventricular septum), constitute the *skeleton of the heart* (fig. 13.6*b*).

## Blood Flow Through the Heart

Blood low in oxygen and high in carbon dioxide enters the right atrium through the venae cavae and the coronary sinus. As the right atrial wall contracts, the blood passes through the tricuspid valve and enters the chamber of

**TABLE 13.1 Heart Valves**

| Valve | Location | Function |
|---|---|---|
| Tricuspid valve | Opening between right atrium and right ventricle | Prevents blood from moving from the right ventricle into the right atrium during ventricular contraction |
| Pulmonary valve | Entrance to pulmonary trunk | Prevents blood from moving from the pulmonary trunk into the right ventricle during ventricular relaxation |
| Mitral (bicuspid) valve | Opening between left atrium and left ventricle | Prevents blood from moving from the left ventricle into the left atrium during ventricular contraction |
| Aortic valve | Entrance to aorta | Prevents blood from moving from the aorta into the left ventricle during ventricular relaxation |

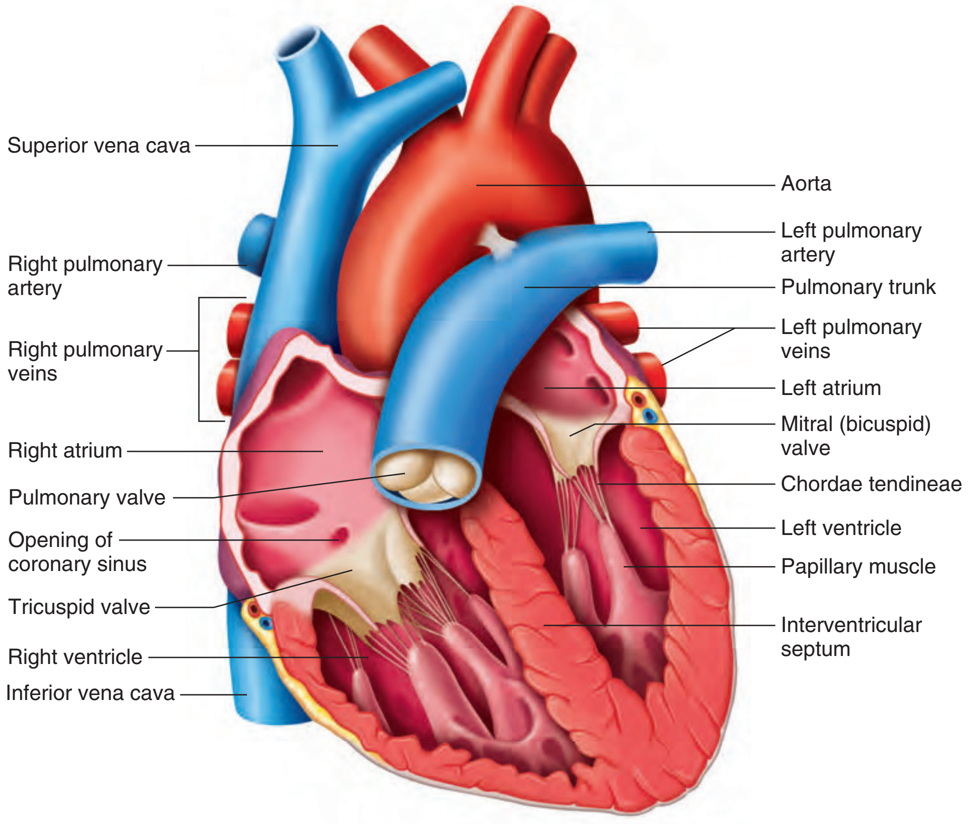
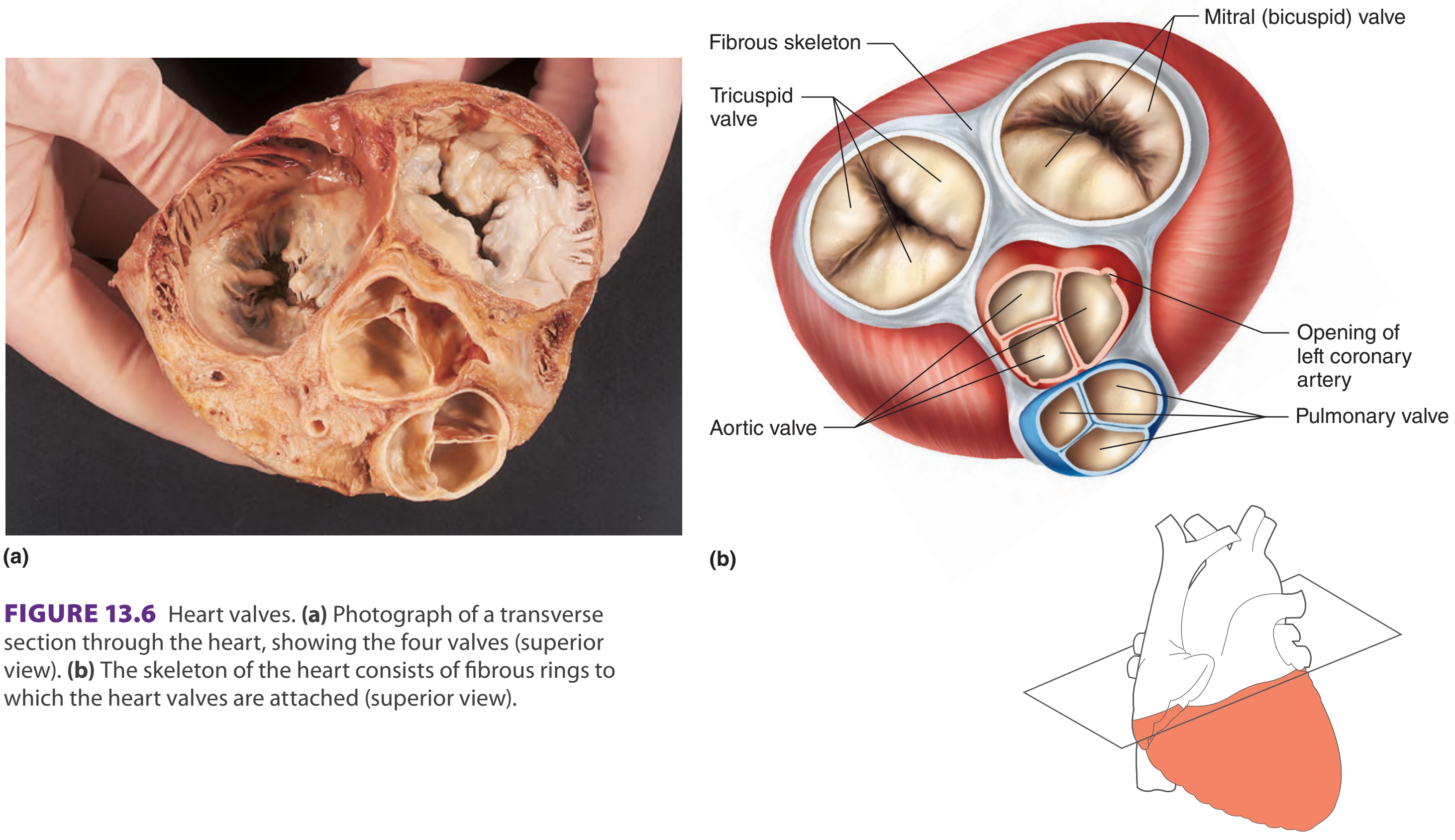

Superior vena cava
Right pulmonary artery
Right pulmonary veins
Right atrium
Pulmonary valve
Opening of coronary sinus
Tricuspid valve
Right ventricle
Inferior vena cava
Aorta
Left pulmonary artery
Pulmonary trunk
Left pulmonary veins
Left atrium
Mitral (bicuspid) valve
Chordae tendineae
Left ventricle
Papillary muscle
Interventricular septum

**FIGURE 13.5** APR Frontal section of the heart showing the connection between the right ventricle and the pulmonary trunk, as well as the four hollow chambers. The plane of section does not show the aortic valve, and shows only parts of the tricuspid and mitral valves.


Fibrous skeleton
Tricuspid valve
Mitral (bicuspid) valve
Opening of left coronary artery
Pulmonary valve
Aortic valve

(a)

(b)

**FIGURE 13.6** Heart valves. **(a)** Photograph of a transverse section through the heart, showing the four valves (superior view). **(b)** The skeleton of the heart consists of fibrous rings to which the heart valves are attached (superior view).

the right ventricle (fig. 13.7). When the right ventricular wall contracts, the tricuspid valve closes, and blood passes through the pulmonary valve and into the pulmonary trunk and its branches (pulmonary arteries).

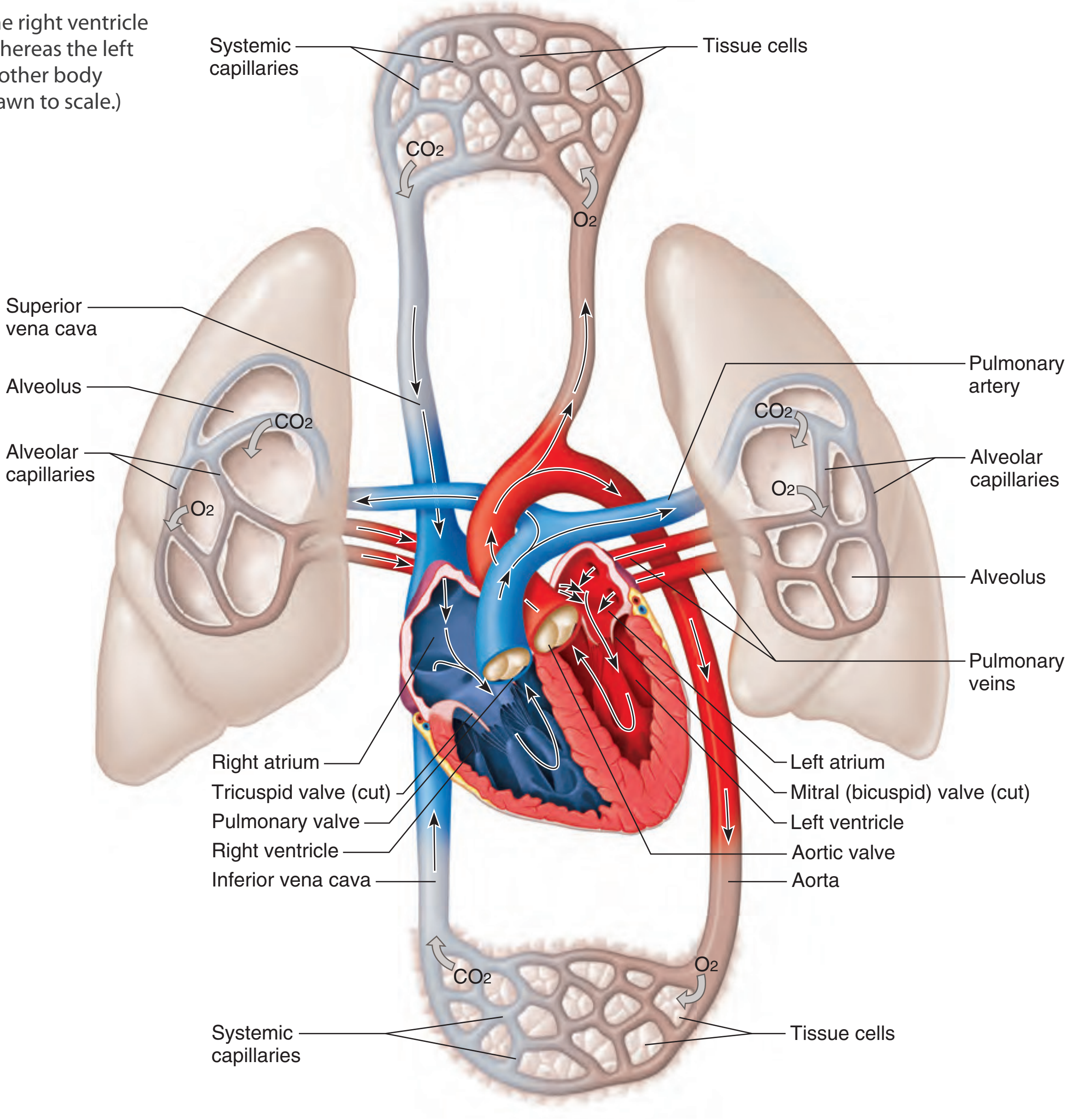
From the pulmonary arteries, blood enters the capillaries associated with the alveoli (microscopic air sacs) of the lungs. Gas exchange occurs between the blood in the capillaries and air in the alveoli. The oxygen-rich blood, now relatively low in carbon dioxide, returns to the heart through the pulmonary veins that lead to the left atrium.

The left atrial wall contracts, and blood moves through the mitral valve and into the chamber of the left ventricle. When the left ventricular wall contracts, the mitral valve closes, and blood passes through the aortic valve and into the aorta and its branches.

In *heart transplantation,* the recipient's failing heart is removed, except for the posterior walls of the right and left atria and their connections to the venae cavae and pulmonary veins. The donor heart is prepared similarly and is attached to the atrial structures remaining in the recipient's thoracic cavity. Finally, the recipient's aorta and pulmonary arteries are connected to those of the donor heart.

Each year in the United States, 3,500 to 4,000 patients are on the waiting list for a heart transplant, but only about 2,100 organs become available. A solution for some people in need of a heart is a left ventricular assist device, or LVAD. The patient wears a battery pack with controls that attach by a cable to the implanted device. LVADs, which began to be developed in the 1980s, are in their third generation. They are now smaller, lighter, with fewer moving parts. The patients with LVADs report improved quality of life—with more energy, better sleep, and improved mood—until they can receive their heart transplants.

**FIGURE 13.7** APR The right ventricle forces blood to the lungs, whereas the left ventricle forces blood to all other body parts. (Structures are not drawn to scale.)


Systemic capillaries
Tissue cells
$CO_2$
$O_2$
Superior vena cava
Alveolus
Alveolar capillaries
$CO_2$
$O_2$
Pulmonary artery
$CO_2$
$O_2$
Alveolar capillaries
Alveolus
Pulmonary veins
Right atrium
Tricuspid valve (cut)
Pulmonary valve
Right ventricle
Inferior vena cava
Left atrium
Mitral (bicuspid) valve (cut)
Left ventricle
Aortic valve
Aorta
$CO_2$
$O_2$
Systemic capillaries
Tissue cells

## Blood Supply to the Heart

The first two branches of the aorta, called the right and left **coronary arteries,** supply blood to the tissues of the heart. Their openings lie just superior to the aortic valve (fig. 13.8). Blood flow through the coronary arteries increases during ventricular relaxation because the myocardial vessels are not compressed as happens in ventricular contraction, and the closed aortic valve does not block the openings to these vessels.

The heart must beat continually to supply blood to body tissues. To do this, myocardial cells require a constant supply of oxygen-rich blood. Branches of the coronary arteries feed the many capillaries of the myocardium (fig. 13.9). The smaller branches of these arteries usually have connections (anastomoses) between vessels that provide alternate pathways for blood, called collateral circulation. These detours in circulation may supply oxygen and nutrients to the myocardium when a coronary artery is blocked.

A thrombus or embolus that partially blocks or narrows a coronary artery branch causes a decrease in blood flow called *ischemia.* This deprives myocardial cells of oxygen, producing a painful condition called *angina pectoris*. The pain usually happens during physical activity, when oxygen demand exceeds oxygen supply. Pain lessens with rest. Emotional disturbance may also trigger angina pectoris.

Angina pectoris feels like heavy pressure, tightening, or squeezing in the chest, and is usually behind the sternum or in the anterior upper thorax. The pain may radiate to the neck, jaw, throat, left shoulder, left upper limb, back, or upper abdomen. Profuse perspiration (diaphoresis), difficulty breathing (dyspnea), nausea, or vomiting may occur.

A blood clot may completely obstruct a coronary artery (coronary thrombosis), killing tissue in that part of the heart. This is a *myocardial infarction (MI)* or heart attack.

Branches of the **cardiac veins,** whose paths roughly parallel those of the coronary arteries, drain blood that has passed through myocardial capillaries. As figure 13.9*b* shows, these veins join an enlarged vein on the heart's posterior surface—the **coronary sinus**—which empties into the right atrium (see fig. 13.5).

### PRACTICE

7. Review the path of blood through the heart.
8. Which vessels supply blood to the myocardium?
9. How does blood return from the cardiac tissues to the right atrium?

## 13.3 | Heart Actions

The heart chambers function in a coordinated fashion. Their actions are regulated so that atria contract, called atrial **systole** (sis′to-le), while ventricles relax, called ventricular **diastole** (di-as′to-le); then ventricles contract (ventricular systole) while atria relax (atrial diastole). Then the atria and ventricles both relax for a brief interval. This series of events constitutes a complete heartbeat, or **cardiac cycle** (kar′de-ak si′kl).

### Cardiac Cycle

During a cardiac cycle, the pressure in the heart chambers rises and falls (see appendix E, p. 581). These changes open and close the valves, much like a door being blown open or closed by the wind. When pressure in the ventricles is low, early in diastole, the pressure difference between the atria and ventricles opens the AV valves. The ventricles fill. About 70% of the returning blood enters the ventricles prior to contraction, and ventricular pressure gradually increases. During atrial systole, the remaining 30% of returning blood is pushed into the ventricles, and ventricular pressure increases (fig. 13.10*a*). Then, as the ventricles contract, ventricular pressure rises sharply. As soon as the ventricular pressure exceeds the atrial pressure, the AV valves close. At the same time, the papillary muscles contract. By pulling on the chordae tendineae, they prevent the cusps of the AV valves from bulging too far into the atria.

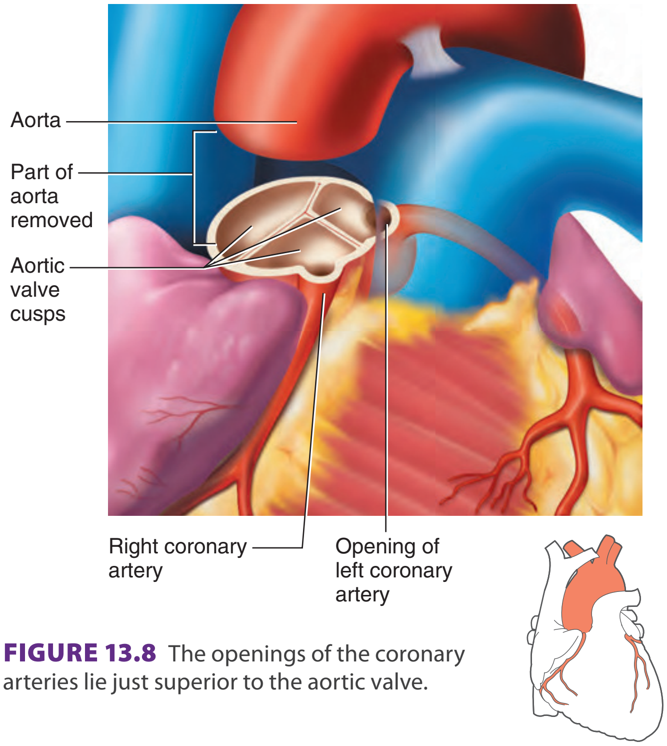


**FIGURE 13.8** The openings of the coronary arteries lie just superior to the aortic valve.

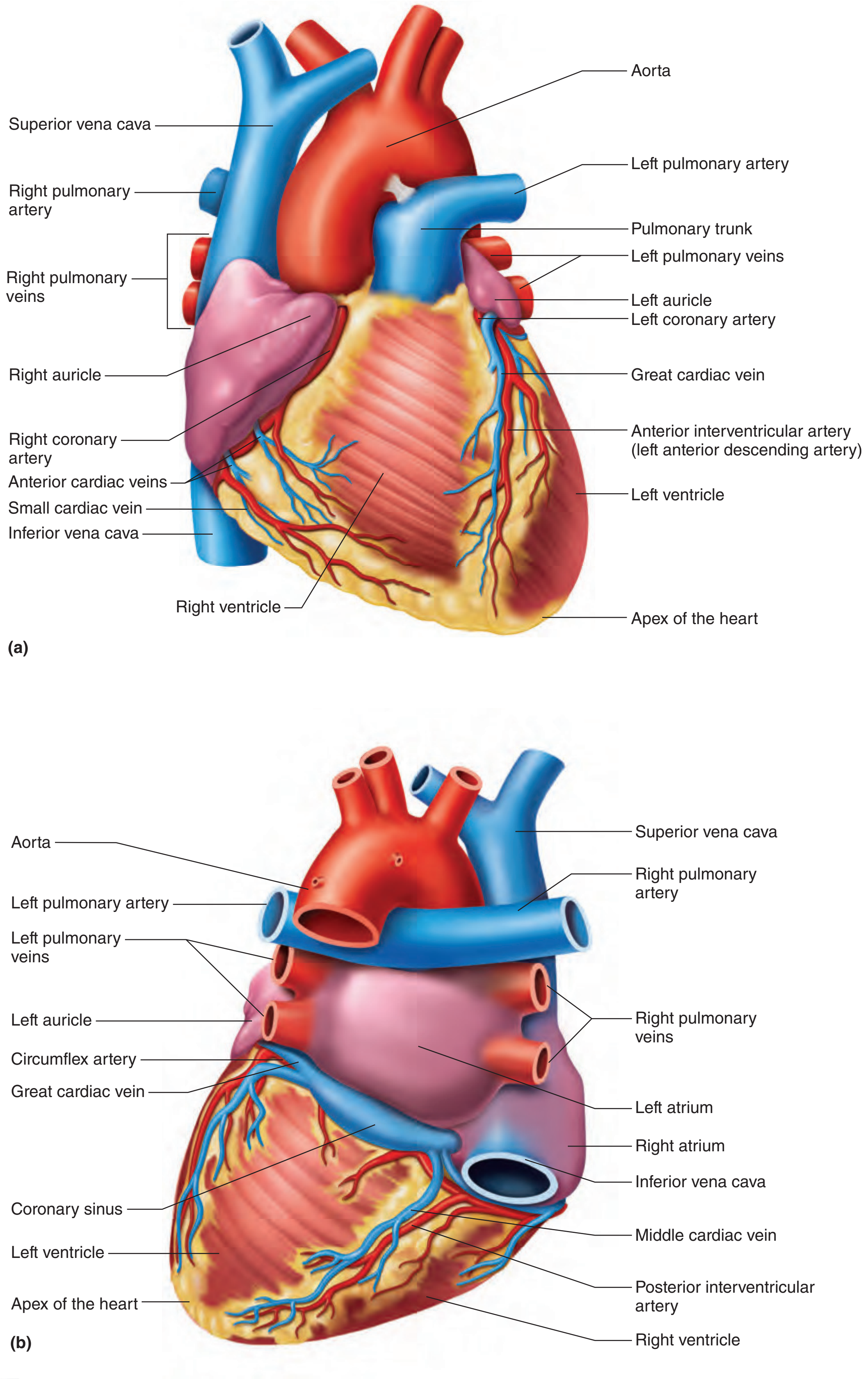

Aorta
Superior vena cava
Left pulmonary artery
Right pulmonary artery
Pulmonary trunk
Left pulmonary veins
Right pulmonary veins
Left auricle
Left coronary artery
Right auricle
Great cardiac vein
Right coronary artery
Anterior interventricular artery (left anterior descending artery)
Anterior cardiac veins
Small cardiac vein
Left ventricle
Inferior vena cava
Right ventricle
Apex of the heart
(a)
Aorta
Superior vena cava
Right pulmonary artery
Left pulmonary artery
Left pulmonary veins
Left auricle
Right pulmonary veins
Circumflex artery
Great cardiac vein
Left atrium
Right atrium
Inferior vena cava
Coronary sinus
Middle cardiac vein
Left ventricle
Posterior interventricular artery
Apex of the heart
Right ventricle
(b)

**FIGURE 13.9** APR Blood vessels associated with the surface of the heart. **(a)** Anterior view. **(b)** Posterior view.

During ventricular systole, the AV valves remain closed. The atria are now relaxed, and pressure in the atria is low, even lower than venous pressure. As a result, blood flows into the atria from the large, attached veins. That is, as the ventricles are contracting, the atria are filling, already preparing for the next cardiac cycle (fig. 13.10*b*).

As ventricular systole progresses, ventricular pressure continues to increase until it exceeds the pressure in the pulmonary trunk (right side) and aorta (left side). At this point, the pressure differences across the semilunar valves open the pulmonary and aortic valves, and blood is ejected from each valve's respective ventricle into these arteries.

As blood flows out of the ventricles, ventricular pressure begins to drop, and it falls even further as the ventricles relax. When ventricular pressure is lower than the blood pressure in the aorta and pulmonary trunk, the pressure difference is reversed, and the semilunar valves close. The ventricles continue to relax, and as soon as ventricular pressure is less than atrial pressure, the AV valves open, and the ventricles begin to fill once more. Atria and ventricles relax for a brief interval.

## Heart Sounds

A heartbeat heard through a stethoscope sounds like *lubb-dupp*. These sounds are due to vibrations in the heart tissues associated with the valves closing.

The first part of a heart sound (*lubb*) originates during ventricular systole, when the AV valves are closing. The second part (*dupp*) occurs during ventricular diastole, when the pulmonary and aortic valves are closing.

Heart sounds provide information about the condition of the heart valves. For example, inflammation of the endocardium (endocarditis) may erode the edges of the valvular cusps. As a result the cusps may not close completely and some blood may leak back through the valve, producing an abnormal sound called a *murmur*. The seriousness of a murmur depends on the degree of valvular damage. Many heart murmurs are harmless. Open heart surgery may be needed to repair or replace severely damaged valves.

## Cardiac Muscle Fibers

Cardiac muscle fibers function like those of skeletal muscles, but the fibers connect in branching networks. The intercalated discs join cardiac muscle cells, allowing action potentials to spread throughout a network of cells that contracts as a unit.

A mass of merging cells that act as a unit is called a **functional syncytium** (funk′shun-al sin-sish′e-um). Two such structures are in the heart—in the atrial walls and in the ventricular walls. Portions of the heart's fibrous skeleton separate these masses of cardiac muscle fibers, except for a small area in the right atrial floor. In this region, fibers of the cardiac conduction system connect the *atrial syncytium* and the *ventricular syncytium*.

### PRACTICE

10. Describe the pressure changes in the atria and ventricles during a cardiac cycle.
11. What causes heart sounds?
12. What is a functional syncytium?

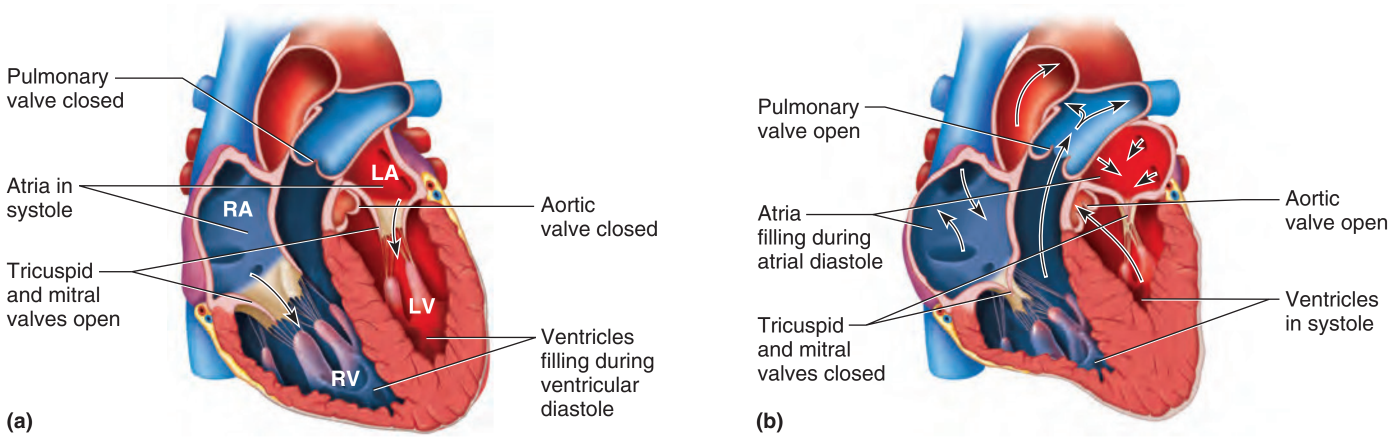

Pulmonary valve closed
Atria in systole
Tricuspid and mitral valves open
LA
RA
LV
RV
Aortic valve closed
Ventricles filling during ventricular diastole
(a)
Pulmonary valve open
Atria filling during atrial diastole
Tricuspid and mitral valves closed
Aortic valve open
Ventricles in systole
(b)

**FIGURE 13.10** APR A cardiac cycle. The atria **(a)** empty during atrial systole and **(b)** fill with blood during atrial diastole.

## Cardiac Conduction System

Throughout the heart are clumps and strands of specialized cardiac muscle tissue whose fibers contain only a few myofibrils. Instead of contracting, these areas initiate and distribute impulses throughout the myocardium. They form the **cardiac conduction system** (kar′de-ak kon-duk′shun sis′tem), which coordinates the events of the cardiac cycle (fig. 13.11).

A key portion of the cardiac conduction system is the **SA node,** or **sinoatrial node,** which is a small elongated mass of specialized cardiac muscle tissue located just beneath the epicardium in the right atrium near the opening of the superior vena cava. Its fibers are continuous with those of the atrial syncytium.

The cells of the SA node can reach threshold on their own, and their cell membranes contact one another. Without stimulation from nerve fibers or any other outside agents, the nodal cells initiate cardiac impulses that spread through preferential pathways into the surrounding myocardium and stimulate cardiac muscle fibers to contract.

SA node activity is rhythmic, initiating one cardiac impulse after another, seventy to eighty times a minute in an adult. Because it generates the heart's rhythmic contractions, the SA node is also called the **pacemaker.**

Figure 13.12 traces the path of a cardiac impulse. As a cardiac impulse from the SA node reaches the atrial syncytium, the right and left atria begin to contract almost simultaneously. The cardiac impulse is not conducted directly into the ventricular syncytium, which is separated from the atrial syncytium by the fibrous skeleton of the heart. Instead, the cardiac impulse passes along fibers (junctional fibers) of the conduction system that lead to a mass of specialized cardiac muscle tissue called the **AV node,** or **atrioventricular node.** This node is in the inferior part of the septum that separates the atria (interatrial septum) and just beneath the endocardium. It provides the only normal conduction pathway between the atrial and ventricular syncytia.

The junctional fibers that conduct the cardiac impulse into the AV node have small diameters, and because small fibers conduct impulses slowly, they delay transmission. Therefore, the impulse is delayed further as it moves through the AV node. This allows time for the atria to contract completely so they empty all their blood into the ventricles before they contract.

Once the cardiac impulse reaches the distal side of the AV node, it passes into a group of large fibers that make up the **AV bundle** (bundle of His). The AV bundle enters the upper part of the interventricular septum and divides into right and left bundle branches that lie just beneath the endocardium. About halfway down the septum, the branches give rise to enlarged **Purkinje fibers** (pur-kin′je fi′berz). The AV bundle and Purkinje fibers conduct the impulse rapidly.

Purkinje fibers spread from the interventricular septum into the papillary muscles, which project inward from ventricular walls and then continue downward to the apex of the heart. There they curve around the tips of the ventricles and pass upward over the lateral walls of these chambers. Along the way, the Purkinje fibers give off many small branches, which become continuous with cardiac muscle fibers.

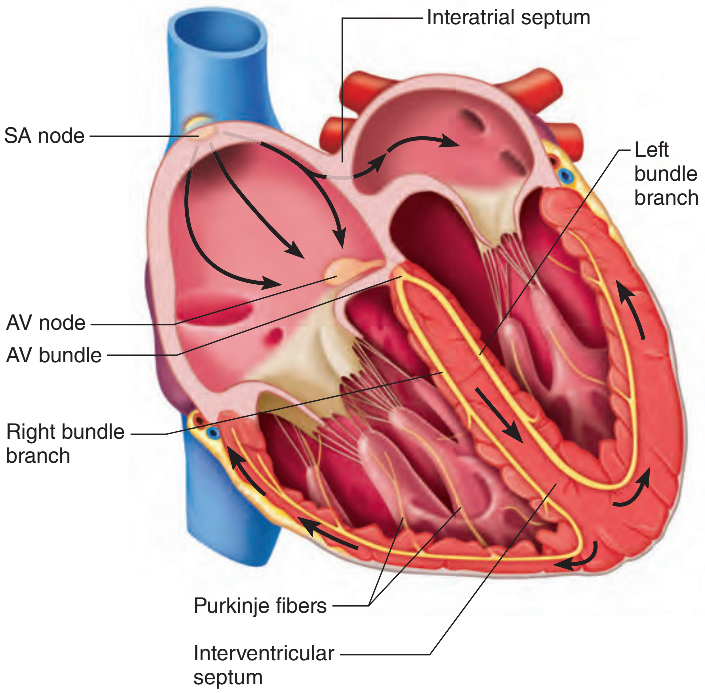


**FIGURE 13.11** APR Components of the cardiac conduction system.

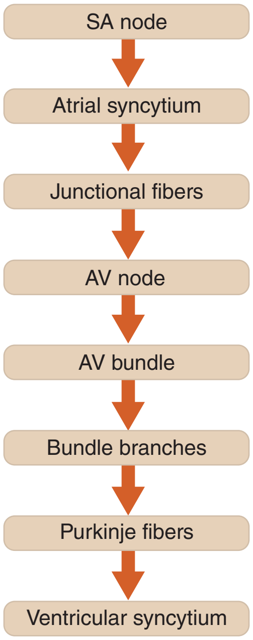


**FIGURE 13.12** Path of a cardiac impulse.

The muscle fibers in ventricular walls form irregular whorls. When impulses on the Purkinje fibers stimulate these muscle fibers, the ventricular walls contract with a twisting motion (fig. 13.13). This action squeezes blood out of the ventricular chambers and forces it into the aorta and pulmonary trunk.

### PRACTICE

13 What types of tissues make up the cardiac conduction system?

14. How is a cardiac impulse initiated?

15. How is a cardiac impulse conducted from the right atrium to the other heart chambers?

## Electrocardiogram

An **electrocardiogram** (e-lek″tro-kar′de-o-gram″), or **ECG,** is a recording of the electrical changes in the myocardium during a cardiac cycle. (This pattern is generated as action potentials stimulate cardiac muscle fibers to contract, but it is not the same as individual action potentials.) These changes are detectable on the surface of the body because body fluids can conduct electrical currents.

To record an ECG, electrodes are placed on the skin and connected by wires to an instrument that responds to small electrical changes. These changes are recorded on a moving strip of paper. Up-and-down movements, or deflections from the baseline, correspond to electrical changes in the myocardium. The paper moves at a known rate, so the distance between deflections indicates the time elapsing between phases of the cardiac cycle.

As figure 13.14*a* illustrates, a normal ECG pattern includes several deflections, or *waves,* during each cardiac cycle. Between cycles, the muscle fibers remain polarized, with no detectable electrical changes, producing a baseline along the moving strip of paper. When the SA node triggers a cardiac impulse, the atrial fibers depolarize, producing an electrical change. A deflection occurs, and at the end of the electrical change the recording returns to the baseline position. This first deflection produces a *P wave,* corresponding to depolarization of the atrial fibers that will lead to contraction of the atria (fig. 13.14*b*).

When the cardiac impulse reaches the ventricular fibers, they rapidly depolarize. The ventricular walls are thicker than those of the atria, so the electrical change is greater, and a greater deflection is recorded. When the electrical change ends, the recording returns to the baseline, leaving a pattern called the *QRS complex* (fig. 13.14*b*). The complex corresponds to depolarization of ventricular fibers just prior to the contraction of the ventricular walls. The record of atrial repolarization seems to be missing from the pattern because atrial fibers repolarize at the same time that ventricular fibers depolarize. Thus, the QRS complex obscures the recording of atrial repolarization. The electrical changes occurring as the ventricular muscle fibers repolarize slowly produce a *T wave* as deflection occurs again. This ends the ECG pattern (fig. 13.14*b*).

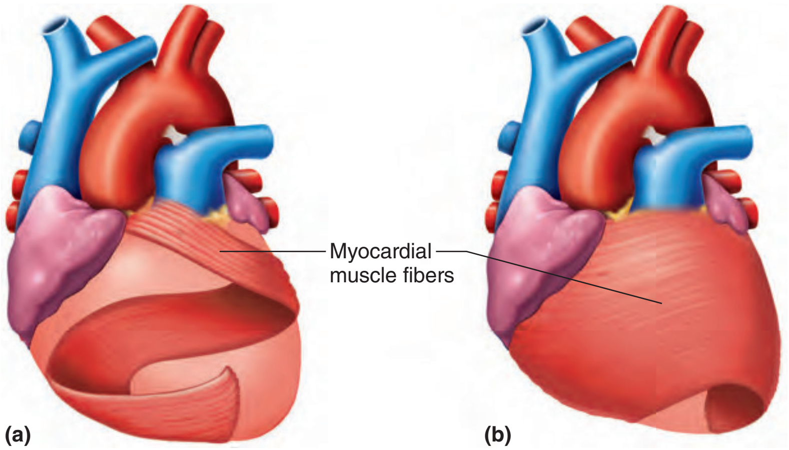


**FIGURE 13.13** AP|R The muscle fibers within the ventricular walls form whorled patterns. The fibers of groups **(a)** and **(b)** surround both ventricles in these anterior views of the heart.

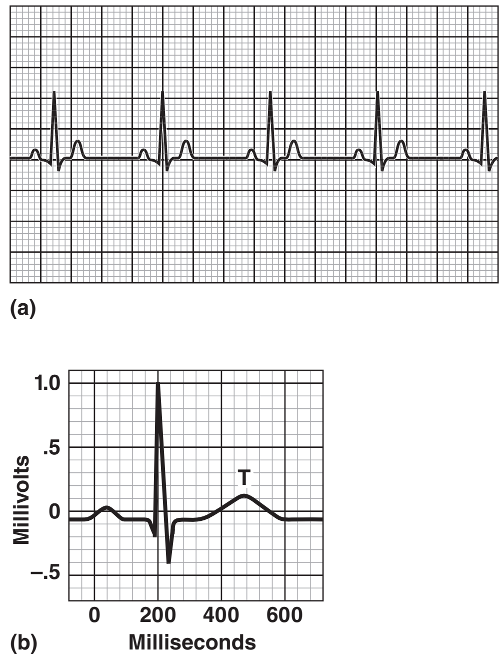


**FIGURE 13.14** AP|R An electrocardiogram records electrical changes in the myocardium during a cardiac cycle. **(a)** A normal ECG. **(b)** In an ECG pattern, the P wave results from a depolarization of the atria, the QRS complex results from a depolarization of the ventricles, and the T wave results from a repolarization of the ventricles.

Q *Which two electrical events occur during the QRS complex?*
**The answer can be found in Appendix F on page 582.**

Physicians use ECG patterns to assess the heart's ability to conduct impulses. For example, the period between the beginning of a P wave and the beginning of a QRS complex, called the *PQ interval* (or if a Q wave is not visible, the PR interval), indicates the time for the cardiac impulse to travel from the SA node through the AV node. Ischemia or other problems affecting the fibers of the AV conduction pathways can prolong this PQ interval. Similarly, injury to the AV bundle can extend the QRS complex, because it may take longer for an impulse to spread throughout the ventricular walls (fig. 13.15).

**PRACTICE**

16. What is an electrocardiogram?
17. Which cardiac events do the P wave, QRS complex, and T wave represent?

## Regulation of the Cardiac Cycle

The volume of blood pumped changes to accommodate cellular requirements. For example, during strenuous exercise, skeletal muscles require more blood, and the heart rate increases in response. Changes in heart rate are often a response to factors that affect the SA node, such as the motor impulses conducted on the parasympathetic and sympathetic nerve fibers (see chapter 9, p. 262). Both divisions of the autonomic nervous system innervate various structures throughout the heart, including the SA node, AV node, and myocardium.

The parasympathetic fibers that innervate the heart arise from neurons in the medulla oblongata and synapse with postganglionic fibers in the wall of the heart (fig. 13.16). When stimulated, the postganglionic fibers release acetylcholine, which decreases SA nodal activity. As a result, the heart rate decreases.

Parasympathetic fibers conduct impulses continually to the SA node, "braking" heart action. Consequently, parasympathetic activity can change heart rate in either direction. An increase in the impulses slows the heart rate, and a decrease in the impulses releases the parasympathetic "brake" and increases the heart rate.

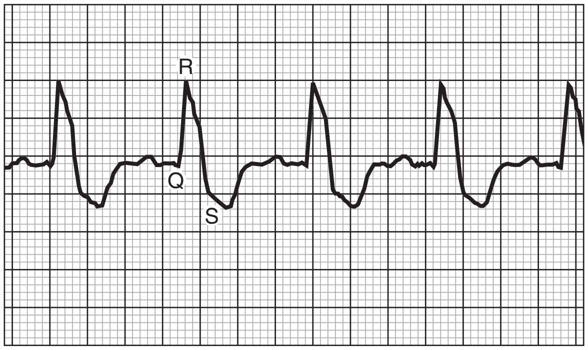


**FIGURE 13.15** A prolonged QRS complex may result from damage to the AV bundle fibers.

Postganglionic sympathetic neurons respond to stimulation by secreting the neurotransmitter norepinephrine. Norepinephrine increases the rate and force of myocardial contractions.

Reflexes called *baroreceptor reflexes* arising from the *cardiac control center* of the medulla oblongata maintain balance between the inhibitory effects of parasympathetic fibers and the excitatory effects of sympathetic fibers. This center receives sensory information and relays motor impulses to the heart and blood vessels in response. For example, receptors sensitive to stretch are located in certain regions of the aorta (aortic arch) and in the carotid arteries (carotid sinuses) (fig. 13.16). These receptors, called *baroreceptors* (pressoreceptors), can detect changes in blood pressure. Rising blood pressure stretches the receptors, and they signal the cardioinhibitor center in the medulla oblongata. In response, the medulla oblongata sends parasympathetic impulses to the heart, decreasing heart rate. This action helps lower blood pressure toward normal.

Impulses from the cerebrum or hypothalamus also influence the cardiac control center. These impulses may decrease heart rate, such as occurs when a person faints following an emotional upset, or they may increase heart rate during a period of anxiety.

Two other factors that influence heart rate are temperature change and certain ions. Rising body temperature increases heart action, which is why heart rate usually increases during fever. Abnormally low body temperature decreases heart action.

The most important ions that influence heart action are potassium ($K^+$) and calcium ($Ca^{+2}$). An excess of potassium ions in the blood (*hyperkalemia*) decreases the rate and force of contractions. If the potassium ion concentration in the blood drops below normal (*hypokalemia*), the heart may develop a potentially life-threatening abnormal rhythm (arrhythmia).

An excess of calcium ions in the blood (*hypercalcemia*) increases heart action, which can result in dangerously extended heart contractions. Conversely, a low blood calcium concentration (*hypocalcemia*) depresses heart action.

An abnormally fast heartbeat, more than 100 beats per minute at rest, is called *tachycardia.* Increase in body temperature, nodal stimulation by sympathetic fibers, certain drugs or hormones, heart disease, excitement, exercise, anemia, or shock can cause tachycardia.

*Bradycardia* means a slow heart rate, fewer than 60 beats per minute. Decreased body temperature, nodal stimulation by parasympathetic impulses, or certain drugs may cause bradycardia. It may also occur during sleep.

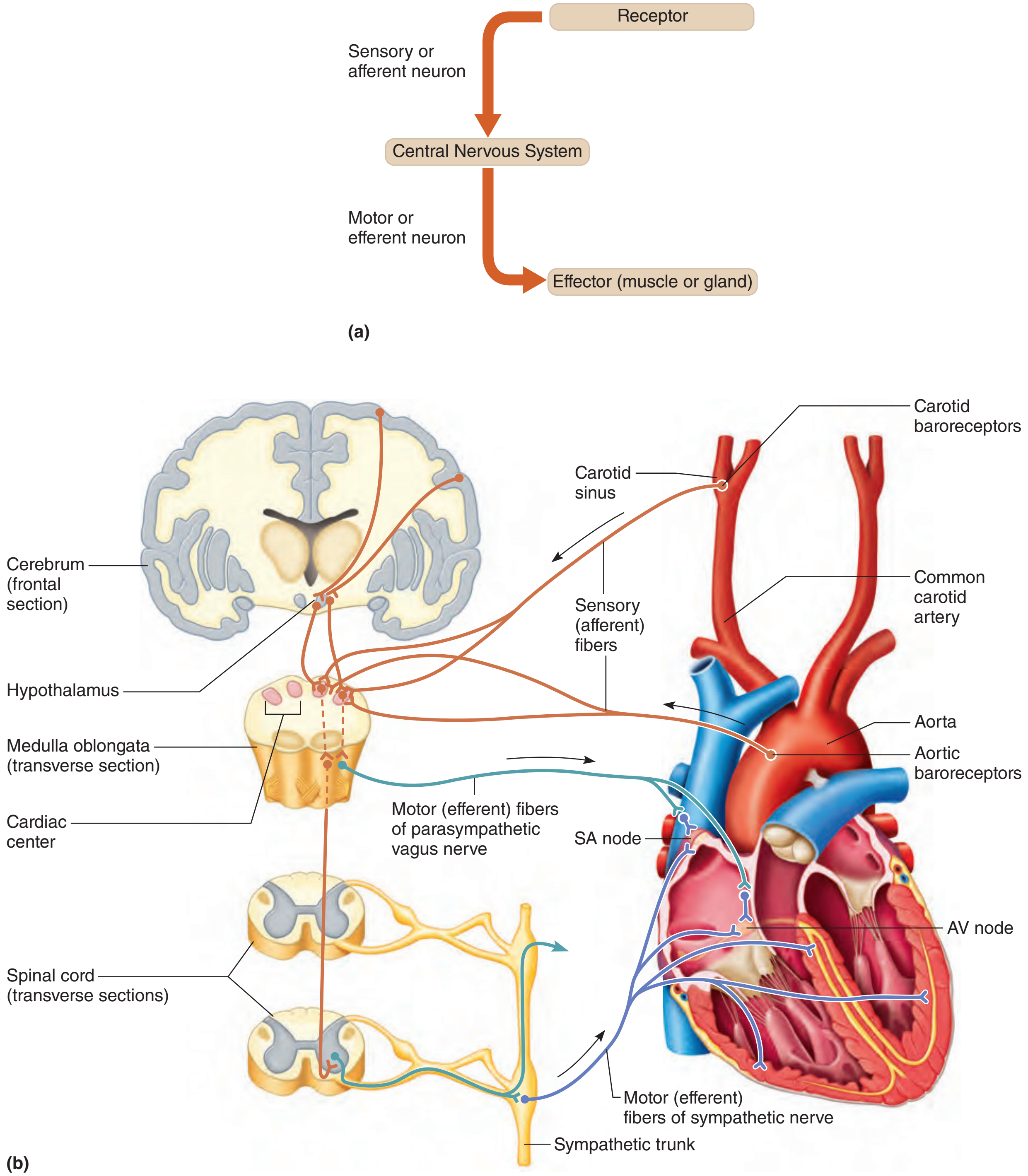

Receptor
Sensory or afferent neuron
Central Nervous System
Motor or efferent neuron
Effector (muscle or gland)
(a)
Carotid baroreceptors
Carotid sinus
Cerebrum (frontal section)
Sensory (afferent) fibers
Common carotid artery
Hypothalamus
Medulla oblongata (transverse section)
Aorta
Aortic baroreceptors
Cardiac center
Motor (efferent) fibers of parasympathetic vagus nerve
SA node
AV node
Spinal cord (transverse sections)
Motor (efferent) fibers of sympathetic nerve
Sympathetic trunk
(b)

**FIGURE 13.16** APR Baroreceptor reflexes. **(a)** Schematic of a general reflex arc. Note the similarity to figure 1.5 on page 14. **(b)** Autonomic nerve impulses alter the activities of the SA and AV nodes.

## PRACTICE

18. How do parasympathetic and sympathetic impulses help control heart rate?
19. How do changes in body temperature affect heart rate?
20. Describe the effects on the heart of abnormal concentrations of potassium and calcium ions.

## 13.4 | Blood Vessels

The blood vessels form a closed circuit of tubes that carries blood from the heart to the body cells and back. These vessels include arteries, arterioles, capillaries, venules, and veins.

**FACTS OF LIFE** The 62,000 or so miles of blood vessels in an average human body would wrap two and a half times around Earth if extended end-to-end.

## Arteries and Arterioles

**Arteries** are strong, elastic vessels adapted for carrying blood away from the heart under relatively high pressure. These vessels subdivide into progressively thinner tubes and eventually give rise to finer, branched **arterioles** (ar-te′re-olz).

The wall of an artery consists of three distinct layers (fig. 13.17*a*). The innermost layer (*tunica interna*) is composed of a layer of simple squamous epithelium, called *endothelium,* that rests on a connective tissue membrane that is rich in elastic and collagen fibers. Endothelium helps prevent blood clotting by providing a smooth surface that allows blood cells and platelets to flow through without being damaged and by secreting biochemicals that inhibit platelet aggregation. Endothelium also may help regulate local blood flow by secreting substances that dilate or constrict blood vessels. For example, endothelium releases the gas nitric oxide, which relaxes the smooth muscle of the vessel. Clinical Application 13.1 describes atherosclerosis, in which fatty deposits accumulate on the inner walls of arteries.

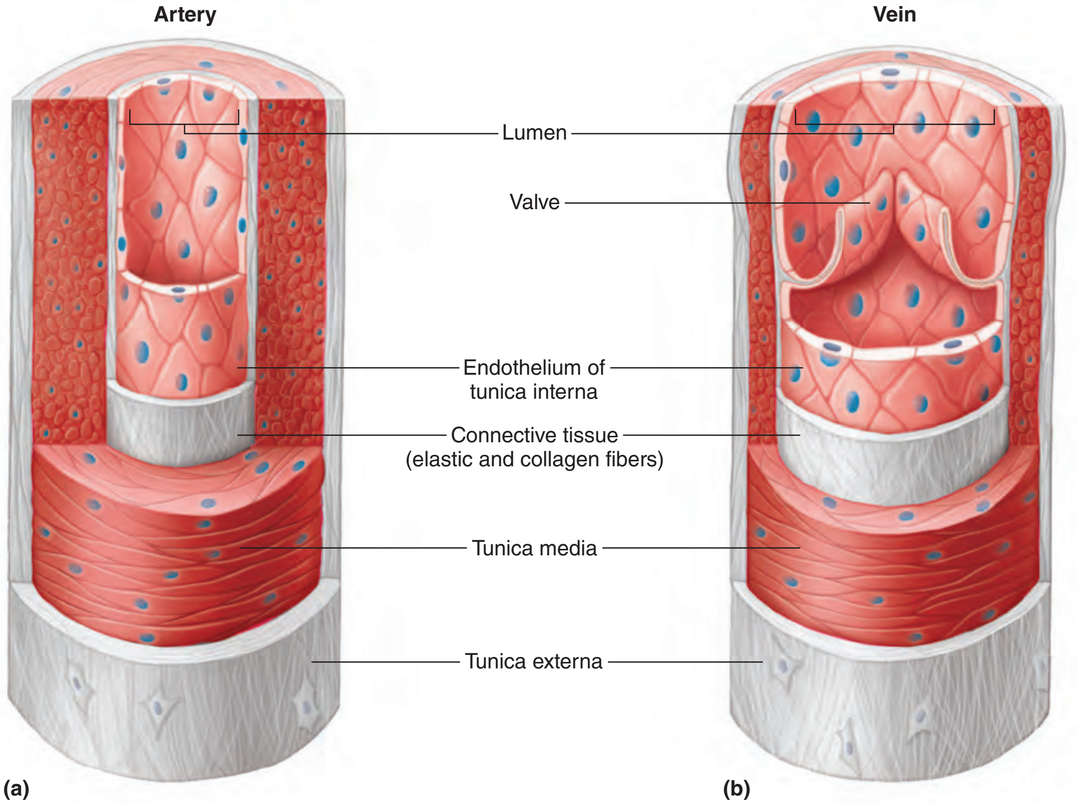
The middle layer (*tunica media*) makes up the bulk of the arterial wall. It includes smooth muscle fibers, which encircle the tube, and a thick layer of elastic connective tissue.

The outer layer (*tunica externa*) is relatively thin and chiefly consists of connective tissue with irregular elastic and collagen fibers. This layer attaches the artery to the surrounding tissues.

If blood pressure dilates a weakened area of an artery wall, a bulge called an *aneurysm* may form and enlarge. If the lining of the vessel tears and allows blood to enter the middle layer of the arterial wall, it is called a *dissecting aneurysm.* An aneurysm may cause symptoms by pressing on nearby organs, or it may rupture and cause great blood loss, which is life-threatening.

Aneurysms may also result from trauma, high blood pressure, certain infections, inherited disorders such as Marfan syndrome, or congenital defects in blood vessels. Common sites of aneurysms include the thoracic and abdominal aorta and an arterial circle at the base of the brain (circle of Willis). Some aneurysms may be treated with a stent, or by replacing the affected part of the vessel with a synthetic graft. A recent technique grafts veins from the patient's own thighs, which are less likely to cause infection or be rejected by the immune system.

The sympathetic branches of the autonomic nervous system innervate smooth muscle in artery and arteriole walls. *Vasomotor fibers* stimulate the smooth muscle to contract, reducing the diameter of the vessel. This is called **vasoconstriction** (vas″o-kon-strik′shun).



Artery
Vein
Lumen
Valve
Endothelium of tunica interna
Connective tissue (elastic and collagen fibers)
Tunica media
Tunica externa
(a)
(b)

**FIGURE 13.17** APR Blood vessels. **(a)** The wall of an artery. **(b)** The wall of a vein.

## CLINICAL APPLICATION 13.1

## Atherosclerosis

In the arterial disease *atherosclerosis* (ath″er-o-sklĕ-ro′sis), deposits of fatty materials, particularly cholesterol, form within and on the inner lining of the arterial walls. Such deposits, called *plaque,* protrude into the lumens of vessels and interfere with blood flow (fig. 13A). Furthermore, plaque often forms a surface texture that can initiate formation of a blood clot, increasing the risk of developing thrombi or emboli that cause decreased blood flow (ischemia) causing tissue death (necrosis) downstream from the obstruction.

Plaque accumulation in coronary arteries may cause a *coronary thrombosis* or *coronary embolism.* Similar changes in brain arteries increase the risk of a *cerebral vascular accident (CVA),* also called a *stroke,* due to cerebral thrombosis, embolism, or hemorrhage. In addition, the walls of affected arteries may degenerate, losing their elasticity and becoming hardened, or *sclerotic.* In this stage of the disease a sclerotic vessel may rupture under the force of blood pressure.

Risk factors for developing atherosclerosis include a fatty diet, elevated blood pressure, tobacco smoking, obesity, and lack of physical exercise. Genetic factors may also increase the risk of developing atherosclerosis.

For millions of people who cannot control cholesterol with diet and exercise, drugs called statins can inhibit a liver enzyme that the body uses to synthesize cholesterol. Statins dramatically reduce LDL cholesterol, and regulate triglyceride levels, lowering the risk of atherosclerosis.

Several invasive treatments attempt to clear clogged arteries. In *percutaneous transluminal angioplasty,* a thin, plastic catheter with a tiny deflated balloon at its tip is passed through an incision in the skin into a large artery in the arm or thigh, guided through other arteries and into the lumen of the affected blood vessel. Once in position at the blockage, the balloon is inflated for several minutes, and this compresses the plaque against the arterial wall, widening the arterial lumen and restoring blood flow. In some cases, the catheter also introduces a stent, which is a coiled steel tube that widens as the balloon inflates, helping to keep the lumen clear. However, blockage can recur if the underlying cause of cholesterol buildup is not addressed.

Lasers are also used to destroy atherosclerotic plaque and to channel through arterial obstructions to increase blood flow. In *laser angioplasty* the laser is passed through an incision in the skin and when it is in the lumen of an obstructed artery, high intensity light energy is transmitted through the optical fibers of the laser.

Another invasive procedure for treating arterial obstruction is *bypass graft surgery.* A surgeon uses a vein or an artery from another part of the patient's body to make a detour around the obstruction. The graft bypasses the narrowed region of the affected artery, supplying blood to the tissues downstream. If a vein is used, the vein is connected backward so that its valves do not impede blood flow. Another technique is to connect the distal end of the left internal mammary artery (LIMA) to the coronary artery beyond the obstruction.

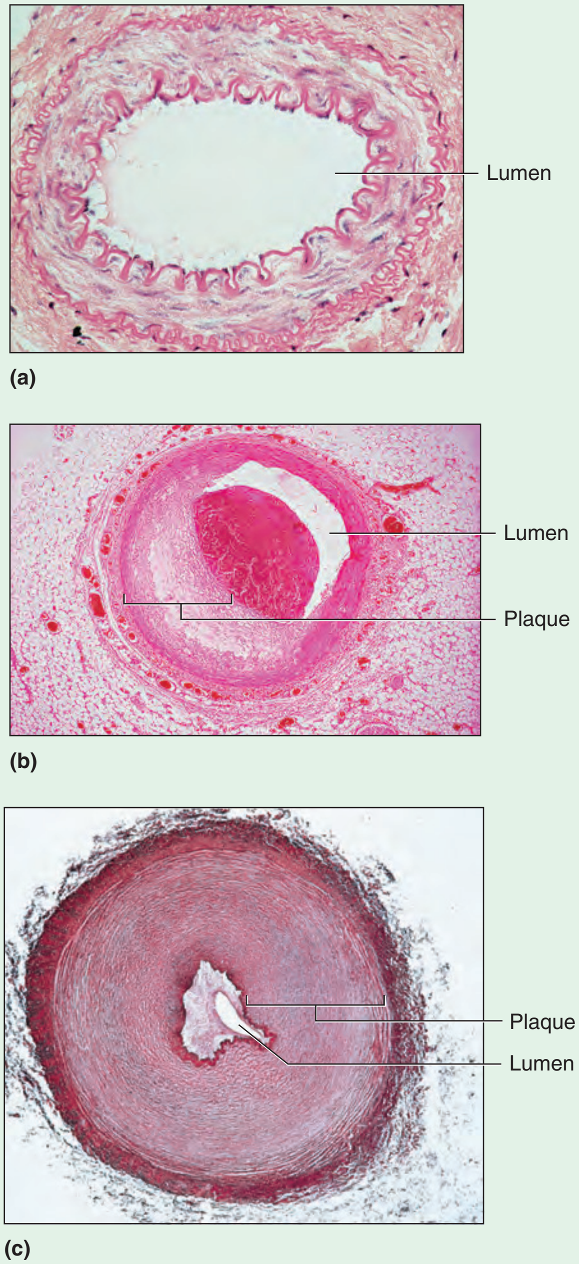


**FIGURE 13A** Development of atherosclerosis. **(a)** Normal arteriole (100×). **(b** and **c)** Accumulation of plaque on the inner wall of an arteriole (100×).

If vasomotor impulses are inhibited, the muscle fibers relax, and the diameter of the vessel increases. This is called **vasodilation** (vas″o-di-la′shun). Changes in the diameters of arteries and arterioles greatly influence blood flow and blood pressure.

The walls of the larger arterioles have three layers, similar to those of arteries. These walls thin as the arterioles approach capillaries. The wall of a very small arteriole consists only of an endothelial lining and some smooth muscle fibers, surrounded by a small amount of connective tissue (fig. 13.18).

## PRACTICE

21. Describe the wall of an artery.
22. What is the function of smooth muscle in the arterial wall?
23. How is the structure of an arteriole different from that of an artery?

## Capillaries

**Capillaries** (kap′ĭ-lar″ēz), the smallest-diameter blood vessels, connect the smallest arterioles and the smallest venules. Capillaries are extensions of the inner linings of arterioles in that their walls are endothelium (fig. 13.18). These thin walls form the semipermeable layer through which substances in the blood are exchanged for substances in the tissue fluid surrounding body cells.

The openings in capillary walls are thin slits where endothelial cells overlap (fig. 13.19). The sizes of these openings and, consequently, the permeability of the capillary wall vary from tissue to tissue. For example, the openings are relatively smaller in capillaries of smooth, skeletal, and cardiac muscle than they are in capillaries associated with endocrine glands, the kidneys, and the lining of the small intestine.

Capillary density reflects tissues' rates of metabolism. Muscle and nerve tissues, which use abundant oxygen and nutrients, are richly supplied with capillaries. Tissues with slower metabolic rates have fewer capillaries, such as cartilage, or lack them entirely, as in the cornea.

The spatial patterns of capillaries also differ in various body parts. For example, some capillaries pass directly from arterioles to venules, but others lead to highly branched networks (fig. 13.20).

Smooth muscle that encircles capillary entrances regulate blood distribution in capillary pathways. These *precapillary sphincters* may close a capillary by contracting or open it by relaxing (see fig. 13.18). A precap-

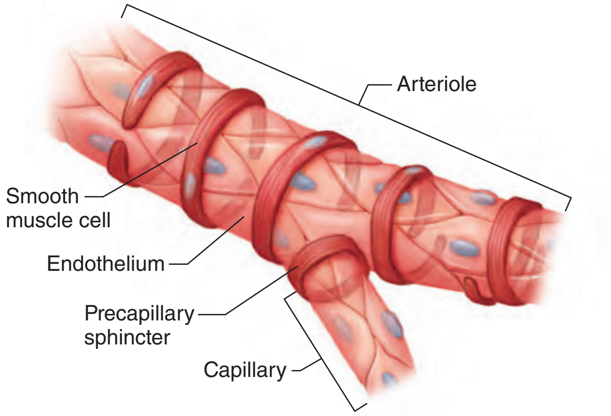


**FIGURE 13.18** The smallest arterioles have only a few smooth muscle fibers in their walls. Capillaries lack these fibers.

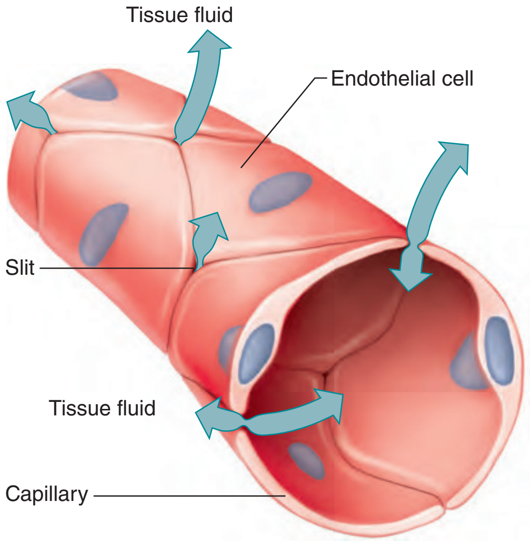


**FIGURE 13.19** In capillaries, substances are exchanged by diffusion between the blood and tissue fluid through openings (slits) separating endothelial cells.

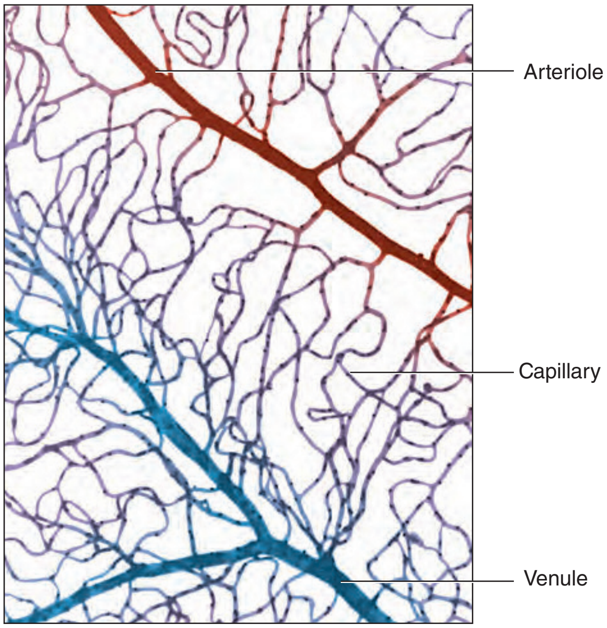


**FIGURE 13.20** Light micrograph of a capillary network (100×).

illary sphincter responds to the demands of the cells the capillary supplies. When these cells have low concentrations of oxygen and nutrients, the sphincter relaxes; when cellular requirements have been met, the sphincter may contract again. In this way, blood flow can follow different pathways through a tissue to meet the changing cellular requirements.

Routing of blood flow to different parts of the body is due to vasoconstriction and vasodilation of arterioles and precapillary sphincters. During exercise, for example, blood enters the capillary networks of the skeletal muscles, where the cells have increased oxygen and nutrient requirements. At the same time, blood can bypass some of the capillary networks in the digestive tract tissues, where demand for blood is less immediate.

**PRACTICE**

24. Describe a capillary wall.
25. What is the function of a capillary?
26. What controls blood flow into capillaries?

### *Exchanges in Capillaries*

Gases, nutrients, and metabolic by-products are exchanged between the blood in capillaries and the tissue fluid surrounding body cells. The substances exchanged move through capillary walls by diffusion, filtration, and osmosis (see chapter 3, pp. 70–75).

Because blood entering systemic capillaries carries high concentrations of oxygen and nutrients, these substances diffuse through the capillary walls and enter the tissue fluid. Conversely, the concentrations of carbon dioxide and other wastes are generally greater in the tissues, and such wastes diffuse into the capillary blood.

Plasma proteins generally remain in the blood because they are too large to diffuse through the membrane channels or the slitlike openings between the endothelial cells of most capillaries. Also, these proteins are not soluble in the lipid parts of capillary cell membranes.

Whereas diffusion depends on concentration gradients, filtration with hydrostatic pressure forces molecules through a membrane. In capillaries, the blood pressure generated when ventricle walls contract provides the force for filtration.

Blood pressure also moves blood through the arteries and arterioles. This pressure decreases as the distance from the heart increases, because of friction (peripheral resistance) between the blood and the vessel walls. For this reason, blood pressure is greater in the arteries than in the arterioles, and greater in the arterioles than in the capillaries. Blood pressure is similarly greater at the arteriolar end of a capillary than at the venular end. Therefore, the filtration effect occurs primarily at the arteriolar ends of capillaries, whereas diffusion takes place along their entire lengths.

The presence of an impermeant solute on one side of a cell membrane creates an osmotic pressure. Plasma proteins trapped in the capillaries create an osmotic pressure that draws water into the capillaries. The term *colloid osmotic pressure* describes this osmotic effect due solely to the plasma proteins.

The effect of capillary blood pressure, which favors filtration, opposes the plasma colloid osmotic pressure, which favors reabsorption. At the arteriolar end of capillaries, the blood pressure is higher than the colloid osmotic pressure, so filtration predominates here. At the venular end, the colloid osmotic pressure is essentially unchanged, but the blood pressure has decreased due to resistance through the capillary, so reabsorption predominates (fig. 13.21).

Normally, more fluid leaves the capillaries than returns to them. Closed-ended vessels called lymphatic capillaries collect the excess fluid and return it through lymphatic vessels to the venous circulation. Chapter 14 (pp. 388–389) discusses this mechanism.

Unusual events may increase blood flow to capillaries, sending excess fluid into the spaces between tissue cells. This may occur in response to certain chemicals, such as *histamine,* that vasodilate the arterioles near capillaries and increase capillary permeability. Enough fluid may leak out of the capillaries to overwhelm lymphatic drainage. Affected tissues become swollen (edematous) and painful.

**PRACTICE**

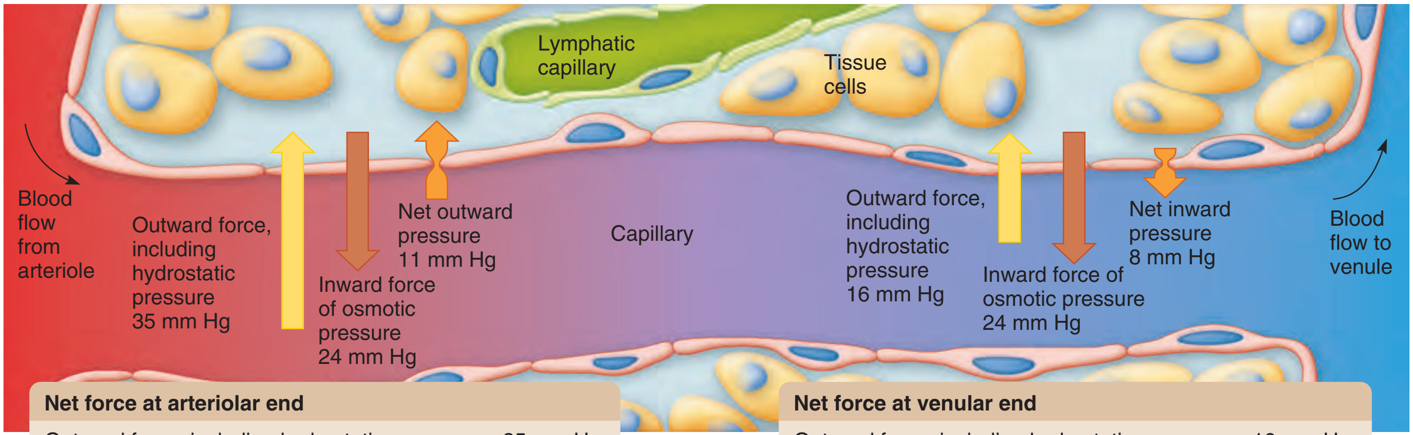
27. Which forces affect the exchange of substances between blood and tissue fluid?
28. Why is the fluid movement out of a capillary greater at its arteriolar end than at its venular end?

## Venules and Veins

**Venules** (ven′ūlz) are the microscopic vessels that continue from the capillaries and merge to form **veins** (vānz). The veins, which carry blood back to the atria, follow pathways that roughly parallel those of the arteries.

The walls of veins are similar to those of arteries in that they are composed of three distinct layers (see fig. 13.17*b*). However, the middle layer of the venous wall is less developed compared to that of the arterial wall. Consequently, veins have thinner walls that have less smooth muscle and less elastic connective tissue than those of comparable arteries, but their lumens have a greater diameter (fig. 13.22).

Many veins, particularly those in the upper and lower limbs, have flaplike *valves,* which project inward from their linings. Most valves are composed of two leaflets


Lymphatic capillary
Tissue cells
Blood flow from arteriole
Outward force, including hydrostatic pressure 35 mm Hg
Inward force of osmotic pressure 24 mm Hg
Net outward pressure 11 mm Hg
Capillary
Outward force, including hydrostatic pressure 16 mm Hg
Inward force of osmotic pressure 24 mm Hg
Net inward pressure 8 mm Hg
Blood flow to venule

| Net force at arteriolar end | |
|---|---|
| Outward force, including hydrostatic pressure | = 35 mm Hg |
| Inward force of osmotic pressure | = 24 mm Hg |
| Net outward pressure | = 11 mm Hg |

| Net force at venular end | |
|---|---|
| Outward force, including hydrostatic pressure | = 16 mm Hg |
| Inward force of osmotic pressure | = 24 mm Hg |
| Net inward pressure | = 8 mm Hg |

**FIGURE 13.21** APR Water and other substances leave capillaries because of a net outward pressure at the capillaries' arteriolar ends. Water enters at the capillaries' venular ends because of a net inward pressure. Substances move in and out along the length of the capillaries according to their respective concentration gradients.

Q *Which substances do not leave the blood at the arteriolar end of the capillary and whose presence at the venular end of the capillary draws water by osmosis back into the capillary?*

**The answer can be found in Appendix F on page 582.**

that close if blood begins to back up in a vein (fig. 13.23). These valves aid in returning blood to the heart because they open as long as the blood flow is toward the heart, but prevent flow in the opposite direction.

Veins also function as blood reservoirs. For example, in hemorrhage accompanied by a drop in arterial blood pressure, sympathetic impulses reflexly stimulate the muscular walls of the veins. The resulting constriction of the veins helps maintain blood pressure by returning more blood to be pumped by the heart. This mechanism ensures a nearly normal blood pressure even when as much as 25% of blood volume is lost. Table 13.2 summarizes the characteristics of blood vessels.

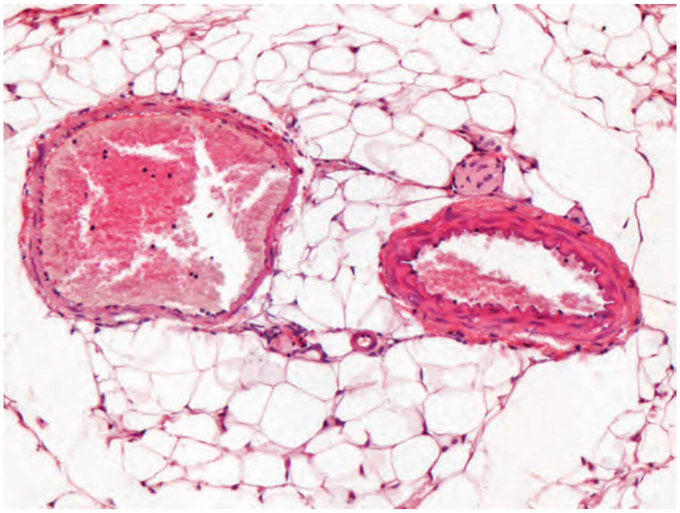


**FIGURE 13.22** APR Note the structural differences in these cross sections of a vein (left) and an artery (right) (60×).

*Varicose veins* are abnormal and irregular dilations in superficial veins, particularly in the legs. This condition is usually associated with prolonged, increased back pressure in the affected vessels due to gravity, as when a person stands. Crossing the legs or sitting in a chair so that its edge presses against the area behind the knee can obstruct venous blood flow and aggravate varicose veins.

Increased venous back pressure stretches and widens the veins. The valves in these vessels lose their ability to block the backward flow of blood, and blood accumulates in the veins. The resulting increased venous pressure is accompanied by rising pressure in the venules and capillaries that supply the veins. Consequently, tissues in affected regions typically become edematous and painful.

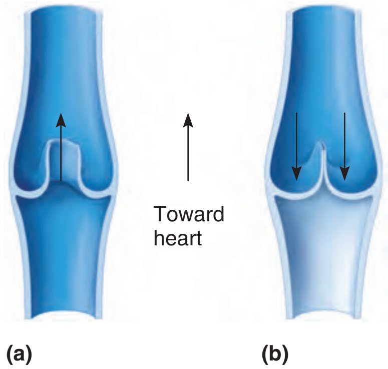

Toward heart
(a)
(b)

**FIGURE 13.23** Venous valves **(a)** allow blood to move toward the heart, but **(b)** prevent blood from moving backward away from the heart.

**TABLE 13.2 Characteristics of Blood Vessels**

| Vessel | Type of Wall | Function |
|---|---|---|
| Artery | Thick, strong wall with three layers—an endothelial lining, a middle layer of smooth muscle and elastic connective tissue, and an outer layer of connective tissue | Carries blood under relatively high pressure from heart to arterioles |
| Arteriole | Thinner wall than an artery but with three layers; smaller arterioles have an endothelial lining, some smooth muscle tissue, and a small amount of connective tissue | Connects an artery to a capillary; helps control blood flow into a capillary by vasoconstricting or vasodilating |
| Capillary | Single layer of squamous epithelium | Allows nutrients, gases, and wastes to be exchanged between the blood and tissue fluid; connects an arteriole to a venule |
| Venule | Thinner wall than in an arteriole, less smooth muscle and elastic connective tissue | Connects a capillary to a vein |
| Vein | Thinner wall than an artery but with similar layers; the middle layer is more poorly developed; some have flaplike valves | Carries blood under relatively low pressure from a venule to the heart; valves prevent backflow of blood; serves as a blood reservoir |

## PRACTICE

29. How does the structure of a vein differ from that of an artery?
30. How does venous circulation help maintain blood pressure when hemorrhaging causes blood loss?

## 13.5 | Blood Pressure

Blood pressure is the force blood exerts against the inner walls of the blood vessels. Although this force occurs throughout the vascular system, the term *blood pressure* most commonly refers to pressure in arteries supplied by branches of the aorta (systemic arteries).

**FACTS OF LIFE** Contraction of the human heart can create enough pressure to squirt blood almost ten feet into the air.

### Arterial Blood Pressure

Arterial blood pressure rises and falls in a pattern corresponding to the phases of the cardiac cycle. That is, contracting ventricles (ventricular systole) squeeze blood out and into the pulmonary trunk and aorta, which sharply increases the pressures in these arteries. The maximum pressure during ventricular contraction is called the **systolic pressure** (sis-tol′ik presh′ur). When the ventricles relax (ventricular diastole), the arterial pressure drops, and the lowest pressure that remains in the arteries before the next ventricular contraction is termed the **diastolic pressure** (di-a-stol′ik presh′ur). A sphygmomanometer is used to measure arterial blood pressure, reporting a fraction that is normally about 120/80. The upper number indicates the arterial systolic pressure in mm Hg (SP), and the lower number indicates the arterial diastolic pressure in mm Hg (DP). Figure 13.24 shows how these pressures decrease as distance from the left ventricle increases.

The surge of blood entering the arterial system during a ventricular contraction distends the elastic arterial walls, but the pressure begins to drop almost immediately as the contraction ends, and the arterial walls recoil. This alternate expanding and recoiling of the arterial wall can be felt as a *pulse* in an artery that runs close to the body surface. The radial artery is commonly used to take a person's pulse. Other sites where an arterial pulse is easily detected include the carotid, brachial, and femoral arteries.

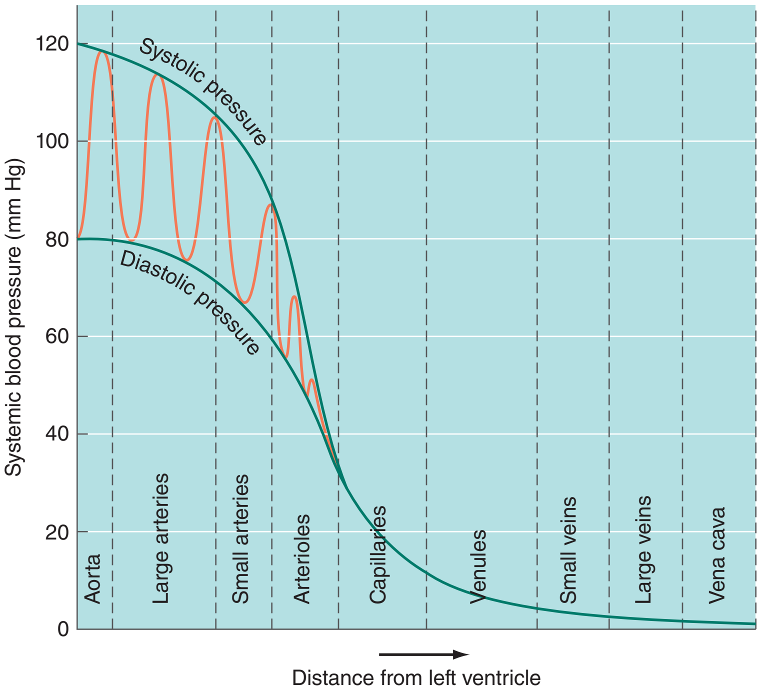


**FIGURE 13.24** Blood pressure decreases as the distance from the left ventricle increases. Systolic pressure occurs during maximal ventricular contraction. Diastolic pressure occurs when the ventricles relax.

**PRACTICE**

31. What is blood pressure?
32. Distinguish between systolic and diastolic blood pressure.
33. What causes a pulse in an artery?

## Factors That Influence Arterial Blood Pressure

Arterial blood pressure depends on a variety of factors. These include cardiac output, blood volume, peripheral resistance, and blood viscosity (fig. 13.25).

### *Cardiac Output*

In addition to producing blood pressure by forcing blood into the arteries, heart action determines how much blood enters the arterial system with each ventricular contraction. The volume of blood discharged from the ventricle with each contraction is called the **stroke volume** and equals about 70 milliliters in an average-weight male at rest. The volume discharged from the ventricle per minute is called the **cardiac output.** It is calculated by multiplying the stroke volume by the heart rate in beats per minute (cardiac output = stroke volume × heart rate). For example, if the stroke volume is 70 milliliters per beat and the heart rate is 72 beats per minute, the cardiac output is 5,040 milliliters per minute.

Blood pressure varies with the cardiac output. If either the stroke volume or the heart rate increases, so does the cardiac output, and blood pressure would increase. Conversely, if the stroke volume or the heart rate decreases, the cardiac output decreases, and blood pressure would decrease.

### *Blood Volume*

**Blood volume** equals the sum of the formed elements and plasma volumes in the vascular system. Although the blood volume varies somewhat with age, body size, and sex, it is usually about 5 liters for adults, or 8% of body weight in kilograms.

Normally blood pressure is directly proportional to blood volume in the cardiovascular system. Thus, any changes in blood volume can initially alter the blood pressure. For example, if a hemorrhage reduces blood volume, blood pressure initially drops. If a transfusion restores normal blood volume, normal blood pressure may be reestablished. Blood volume can also fall if the fluid balance is upset, as happens in dehydration. Fluid replacement can reestablish normal blood volume and pressure.

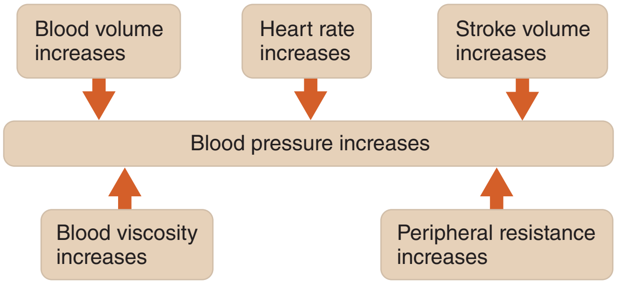


**FIGURE 13.25** Some of the factors that influence arterial blood pressure.

**FACTS OF LIFE** Black licorice contains a sweet-tasting compound called glycyrrhizic acid that can raise blood pressure if a person consumes it in excess.

### *Peripheral Resistance*

Friction between the blood and the walls of blood vessels produces a force called **peripheral resistance** (pĕ-rif′er-al re-zis′tans), which hinders blood flow. Blood pressure must overcome peripheral resistance if the blood is to continue flowing. Factors that alter the peripheral resistance change blood pressure. For example, contracting smooth muscles in arteriolar walls increase the peripheral resistance by constricting these vessels. Blood backs up into the arteries supplying the arterioles, and the arterial pressure rises. Dilation of arterioles has the opposite effect—peripheral resistance decreases, and arterial blood pressure drops in response.

### *Blood Viscosity*

**Viscosity** (vis-kos′ĭ-te) is the difficulty with which the molecules of a fluid flow past one another. The greater the viscosity, the greater the resistance to flow.

Blood cells and plasma proteins increase blood viscosity. The greater the blood's resistance to flowing, the greater the force needed to move it through the vascular system. Thus, it is not surprising that blood pressure rises as blood viscosity increases and drops as viscosity decreases.

**PRACTICE**

34. How are cardiac output and blood pressure related?
35. How does blood volume affect blood pressure?
36. What is the relationship between peripheral resistance and blood pressure? Between blood viscosity and blood pressure?

## Control of Blood Pressure

Blood pressure (BP) is determined by cardiac output (CO) and peripheral resistance (PR) according to this relationship:

$$BP = CO \times PR$$

Maintenance of normal arterial pressure therefore requires regulation of these two factors.

The volume of blood returning to the heart and entering the ventricles affects cardiac output. Entering blood mechanically stretches myocardial fibers in the ventricular walls. Within limits, the longer these fibers, the greater is the force with which they contract. The relationship between fiber length (due to stretching of the cardiac muscle cell just before contraction) and force of contraction is called the *Frank-Starling law of the heart.* This relationship becomes important, for example, during exercise when venous blood returns more rapidly to the heart. The more blood that enters the heart from the veins, the greater the ventricular distension, the stronger the contraction, the greater the amount of blood pumped in a single beat (stroke volume), and the greater the cardiac output. Conversely, the less blood that returns from the veins, the less the ventricle distends, the weaker the ventricular contraction, the lesser the stroke volume and cardiac output. This mechanism ensures that the volume of blood discharged from the heart is equal to the volume entering its chambers.

Cardiac output and peripheral resistance are controlled in part by baroreceptor reflexes. *Baroreceptors* are sensory receptors in the aortic arch and carotid arteries that sense changes in blood pressure. If arterial pressure increases, impulses travel from the baroreceptors to the cardiac center of the medulla oblongata. This center relays parasympathetic impulses to the SA node in the heart, and the heart rate decreases in response. As a result of this *cardioinhibitor reflex,* cardiac output falls, and blood pressure decreases toward the normal level (fig. 13.26). Conversely, decreasing arterial blood pressure initiates the *cardioaccelerator reflex,* which sends sympathetic impulses to the SA node. As a result, the heart beats faster, increasing cardiac output and arterial pressure. Other factors that increase heart rate and blood pressure include exercise, a rise in body temperature, and emotional responses, such as fear and anger. Clinical Application 13.2 discusses the effects of exercise on cardiovascular functioning.

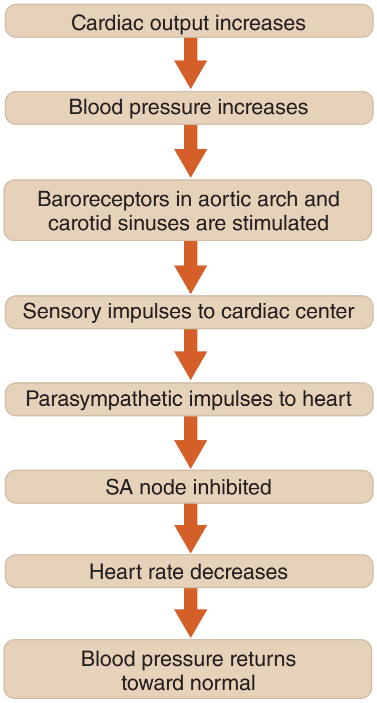

Cardiac output increases
Blood pressure increases
Baroreceptors in aortic arch and carotid sinuses are stimulated
Sensory impulses to cardiac center
Parasympathetic impulses to heart
SA node inhibited
Heart rate decreases
Blood pressure returns toward normal

**FIGURE 13.26** If blood pressure rises, baroreceptors initiate the cardioinhibitor reflex, which lowers the blood pressure.

Peripheral resistance also controls blood pressure. Changes in arteriole diameters regulate peripheral resistance. Because blood vessels with smaller diameters offer a greater resistance to blood flow, factors that cause arteriole vasoconstriction increase peripheral resistance, which raises blood pressure, and factors causing vasodilation decrease peripheral resistance, lowering blood pressure.

The *vasomotor center* of the medulla oblongata continually sends sympathetic impulses to smooth muscle in the arteriole walls, keeping them in a state of tonic contraction. This action helps maintain the peripheral resistance associated with normal blood pressure. Because the vasomotor center responds to changes in blood pressure, it can increase peripheral resistance by increasing its outflow of sympathetic impulses, or it can decrease such resistance by decreasing its sympathetic outflow. In the latter case, the vessels vasodilate as sympathetic stimulation decreases.

Whenever arterial blood pressure suddenly increases, baroreceptors in the aorta and carotid arteries signal the vasomotor center, and the sympathetic outflow to the arterioles falls. The resulting vasodilation decreases peripheral resistance, and blood pressure lowers toward the normal level.

Certain chemicals, including carbon dioxide, oxygen, and hydrogen ions, also influence peripheral resistance by affecting precapillary sphincters and smooth muscle in arteriole walls. For example, increasing blood carbon dioxide, decreasing blood oxygen, and lowering blood pH relaxes smooth muscle in the systemic circulation. This increases local blood flow to tissues with high metabolic rates, such as exercising skeletal muscles. In addition, epinephrine and norepinephrine vasoconstrict many systemic vessels, increasing peripheral resistance.

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*Hypertension,* or high blood pressure, is persistently elevated systemic arterial pressure. It is one of the more common diseases of the cardiovascular system in industrialized nations.

High blood pressure with unknown cause is called *essential* (also primary or idiopathic) *hypertension*. Elevated blood pressure that is a consequence of another problem, such as kidney disease, is called *secondary hypertension*.

The consequences of prolonged, uncontrolled hypertension can be very serious. As the left ventricle works harder to pump blood at a higher pressure, the myocardium thickens, enlarging the heart. If coronary blood flow cannot support this growth, parts of the heart muscle die and fibrous tissue replaces them. Eventually, the enlarged and weakened heart fails to maintain adequate output for survival.

Exercising regularly, maintaining a healthy body weight, reducing stress, and limiting dietary sodium may control blood pressure. If necessary, medications may include diuretics and/or inhibitors of sympathetic nerve action.

CLINICAL APPLICATION **13.2**

## Exercise and the Cardiovascular System

The cardiovascular system adapts to aerobic exercise. The aerobically conditioned athlete or person who exercises regularly experiences increases in heart pumping efficiency, blood volume, blood hemoglobin concentration, and the number of mitochondria in muscle fibers. These adaptations improve oxygen delivery to, and utilization by, muscle tissue.

An athlete's heart typically changes in response to increased demands, and may enlarge 40% or more. Myocardial mass increases, the ventricular cavities expand, and the ventricle walls thicken. At rest, stroke volume increases, and heart rate and blood pressure decrease. To a physician unfamiliar with a conditioned cardiovascular system, a trained athlete may appear abnormal. For example, a prolonged QT interval on an electrocardiogram for a long-time distance runner is not necessarily an indication of "long QT syndrome," as it might be in a less physically fit individual.

The cardiovascular system responds beautifully to a slow, steady buildup in exercise frequency and intensity. It may not react well to sudden demands, such as when a person who never exercises suddenly shovels snow. Sedentary people have a two- to sixfold increased risk of cardiac arrest while exercising than when not; people in shape have little or no excess risk while exercising.

For exercise to benefit the cardiovascular system, the heart rate must be elevated to 70–85% of its "theoretical maximum" for 30 to 60 minutes, at least three to four times a week, according to the American Heart Association. To calculate your theoretical maximum, subtract your age from 220. If you are eighteen years old, your theoretical maximum is 202 beats per minute. Then, 70–85% of this value is 141–172 beats per minute. Some good activities for raising the heart rate are tennis, skating, skiing, handball, vigorous dancing, hockey, basketball, biking, and fast walking.

It is wise to consult a physician before starting an exercise program. People over age thirty are advised to have a stress test, which is an electrocardiogram taken while exercising. (The standard electrocardiogram is taken at rest.) An arrhythmia that appears only during exercise may indicate heart disease that has not yet produced symptoms. The American Heart Association suggests that after a physical exam, a sedentary person wishing to start an exercise program begin with 30 minutes of activity (perhaps broken into two 15-minute sessions at first) at least five times per week.

### PRACTICE

37. What factor affects cardiac output?
38. What is the function of baroreceptors in the aortic arch and carotid arteries?
39. How does the vasomotor center control peripheral resistance?

## Venous Blood Flow

Blood pressure decreases as blood moves through the arterial system and into the capillary networks, so that little pressure remains at the venular ends of capillaries (see fig. 13.24). Instead, blood flow through the venous system is only partly the direct result of heart action and depends on other factors, such as skeletal muscle contraction, breathing movements, and vasoconstriction of veins (*venoconstriction*).

Contracting skeletal muscles press on veins moving blood from one valve section to another (see fig. 13.23). This massaging action of contracting skeletal muscles helps push blood through the venous system toward the heart.

Respiratory movements also move venous blood. During inspiration, the pressure within the thoracic cavity is reduced as the diaphragm contracts and the rib cage moves upward and outward. At the same time, the pressure within the abdominal cavity is increased as the diaphragm presses downward on the abdominal viscera. Consequently, blood is squeezed out of the abdominal veins and forced into thoracic veins. During exercise, these respiratory movements along with skeletal muscle contractions, increase the return of venous blood to the heart.

Venoconstriction also returns venous blood to the heart. When venous pressure is low, sympathetic reflexes stimulate smooth muscle in the walls of veins to contract. The veins provide a blood reservoir that can adapt its capacity to changes in blood volume. If some blood is lost and blood pressure falls, venoconstriction can force blood out of this reservoir. By maintaining venous return to the heart, venoconstriction helps to maintain blood pressure.

### PRACTICE

40. What is the function of venous valves?
41. How do skeletal muscles and respiratory movements affect venous blood flow?
42. What factors stimulate venoconstriction?

## 13.6 | Paths of Circulation

Recall from figure 13.1 that the blood vessels can be divided into two major pathways. The *pulmonary circuit* or pulmonary circulation consists of vessels that carry blood from the heart to the lungs and back to the heart. The *systemic circuit* or systemic circulation carries blood from the heart to all other parts of the body and back. The systemic circuit includes the coronary circulation.

The following sections describe the circulatory pathways after birth. Chapter 20 (pp. 563–564) describes the somewhat different fetal pathways.

### Pulmonary Circuit

Blood enters the pulmonary circuit as it leaves the right ventricle through the pulmonary trunk. The pulmonary trunk extends upward and posteriorly from the heart. About 5 centimeters above its origin, the pulmonary trunk divides into the right and left pulmonary arteries (see fig. 13.5), which penetrate the right and left lungs, respectively. After repeated divisions, the pulmonary arteries give rise to arterioles that continue into the capillary networks associated with the walls of the alveoli, where gas is exchanged between the blood and the air (see chapter 16, pp. 470–471).

From the pulmonary capillaries, blood enters the venules, which merge to form small veins, and these veins in turn converge to form larger veins. Four pulmonary veins, two from each lung, return blood to the left atrium. This completes the vascular loop of the pulmonary circuit.

### Systemic Circuit

Oxygen-rich blood moves from the left atrium into the left ventricle. Contraction of the left ventricle forces this blood into the systemic circuit, which includes the aorta and its branches that lead to all the body tissues, as well as the companion system of veins that returns blood to the right atrium.

**PRACTICE**

43. Distinguish between the pulmonary and systemic circuits of the cardiovascular system.
44. Trace the path of blood through the pulmonary circuit from the right ventricle.

## 13.7 | Arterial System

The **aorta** is the largest-diameter artery in the body. It extends upward from the left ventricle, arches over the heart to the left, and descends just anterior and to the left of the vertebral column. Figure 13.27 shows the aorta and its main branches.

### Principal Branches of the Aorta

The first part of the aorta is called the *ascending aorta.* At the root are the three cusps of the aortic valve, and opposite each cusp is a swelling in the aortic wall called an **aortic sinus.** The right and left coronary arteries arise from two of these sinuses (see fig. 13.8).

Three major arteries originate from the *aortic arch* (arch of the aorta): the **brachiocephalic** (brāk″e-o-sĕ-fal′ik) **artery,** the left **common carotid** (kah-rot′id) **artery,** and the left **subclavian** (sub-kla′ve-an) **artery.**

The upper part of the *descending aorta* is left of the midline. It gradually extends medially and lies directly anterior to the vertebral column at the level of the twelfth thoracic vertebra. The part of the descending aorta above the diaphragm is the **thoracic aorta.** It gives off many small branches to the thoracic wall and the thoracic viscera.

Below the diaphragm, the descending aorta becomes the **abdominal aorta,** and it gives off branches to the abdominal wall and abdominal organs. Branches to abdominal organs include: the **celiac** (se′le-ak) **artery,** which gives rise to the *gastric, splenic,* and *hepatic arteries;* the **superior** (supplies small intestine and superior part of large intestine) and **inferior** (supplies inferior part of large intestine) **mesenteric** (mes″en-ter′ik) **arteries;** and the **suprarenal** (soo″prah-re′nal) **arteries, renal** (re′nal) **arteries,** and **gonadal** (go′nad-al) **arteries,** which supply blood to the adrenal glands, kidneys, and ovaries or testes, respectively. The abdominal aorta ends near the brim of the pelvis, where it divides into right and left **common iliac** (il′e-ak) **arteries.** These vessels supply blood to lower regions of the abdominal wall, the pelvic organs, and the lower extremities. Table 13.3 summarizes the major branches of the aorta.

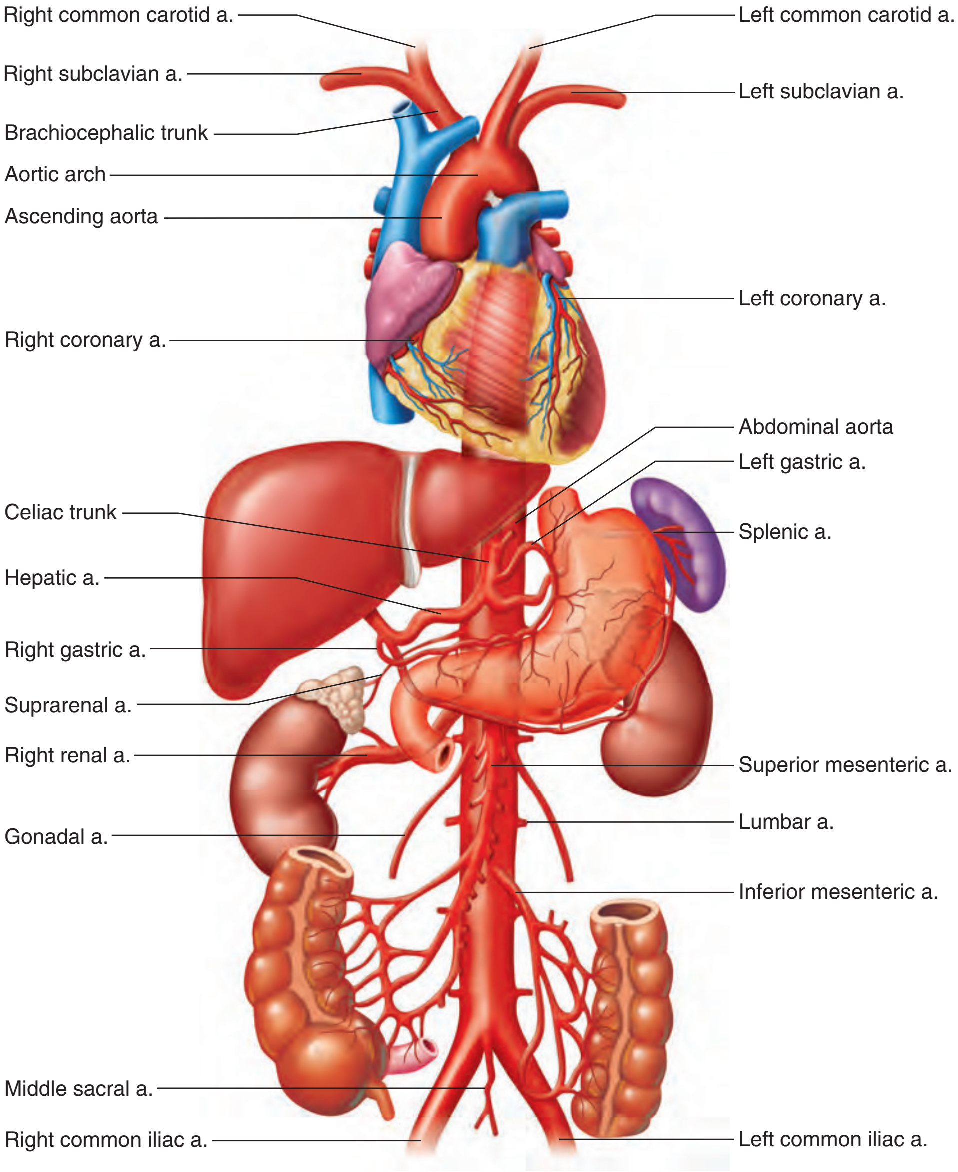
### Arteries to the Neck, Head, and Brain

Branches of the subclavian and common carotid arteries supply blood to structures in the neck, head, and brain (fig. 13.28). The main divisions of the subclavian artery to these regions include the vertebral and thyrocervical arteries. The common carotid artery communicates with these regions by means of the internal and external carotid arteries.

The **vertebral arteries** pass upward through the foramina of the transverse processes of the cervical vertebrae and enter the skull through the foramen magnum. These vessels supply blood to the vertebrae and to their associated ligaments and muscles.

In the cranial cavity, the vertebral arteries unite to form a single *basilar artery.* This vessel passes along the ventral brainstem and gives rise to branches leading to the pons, midbrain, and cerebellum. The basilar artery ends by dividing into two *posterior cerebral arteries* that supply parts of the occipital and temporal lobes of the cerebrum. The posterior cerebral arteries also help form

**FIGURE 13.27** APR Major branches of the aorta. (**a.** stands for **artery.**)


Right common carotid a.
Left common carotid a.
Right subclavian a.
Left subclavian a.
Brachiocephalic trunk
Aortic arch
Ascending aorta
Left coronary a.
Right coronary a.
Abdominal aorta
Left gastric a.
Celiac trunk
Splenic a.
Hepatic a.
Right gastric a.
Suprarenal a.
Right renal a.
Superior mesenteric a.
Lumbar a.
Gonadal a.
Inferior mesenteric a.
Middle sacral a.
Right common iliac a.
Left common iliac a.

## TABLE 13.3 Major Branches of the Aorta

| Portion of Aorta | Branch | General Regions or Organs Supplied |
|---|---|---|
| Ascending aorta | Right and left coronary arteries | Heart |
| Arch of the aorta | Brachiocephalic artery<br>Left common carotid artery<br>Left subclavian artery | Right upper limb, right side of head<br>Left side of head<br>Left upper limb |
| Descending aorta | | |
| Thoracic aorta | Bronchial artery<br>Pericardial artery<br>Esophageal artery<br>Mediastinal artery<br>Posterior intercostal artery | Bronchi<br>Pericardium<br>Esophagus<br>Mediastinum<br>Thoracic wall |
| Abdominal aorta | Celiac artery<br>Phrenic artery<br>Superior mesenteric artery<br>Suprarenal artery<br>Renal artery<br>Gonadal artery<br>Inferior mesenteric artery<br>Lumbar artery<br>Middle sacral artery<br>Common iliac artery | Organs of upper digestive tract<br>Diaphragm<br>Portions of small and large intestines<br>Adrenal gland<br>Kidney<br>Ovary or testis<br>Lower portions of large intestine<br>Posterior abdominal wall<br>Sacrum and coccyx<br>Lower abdominal wall, pelvic organs, and lower limb |

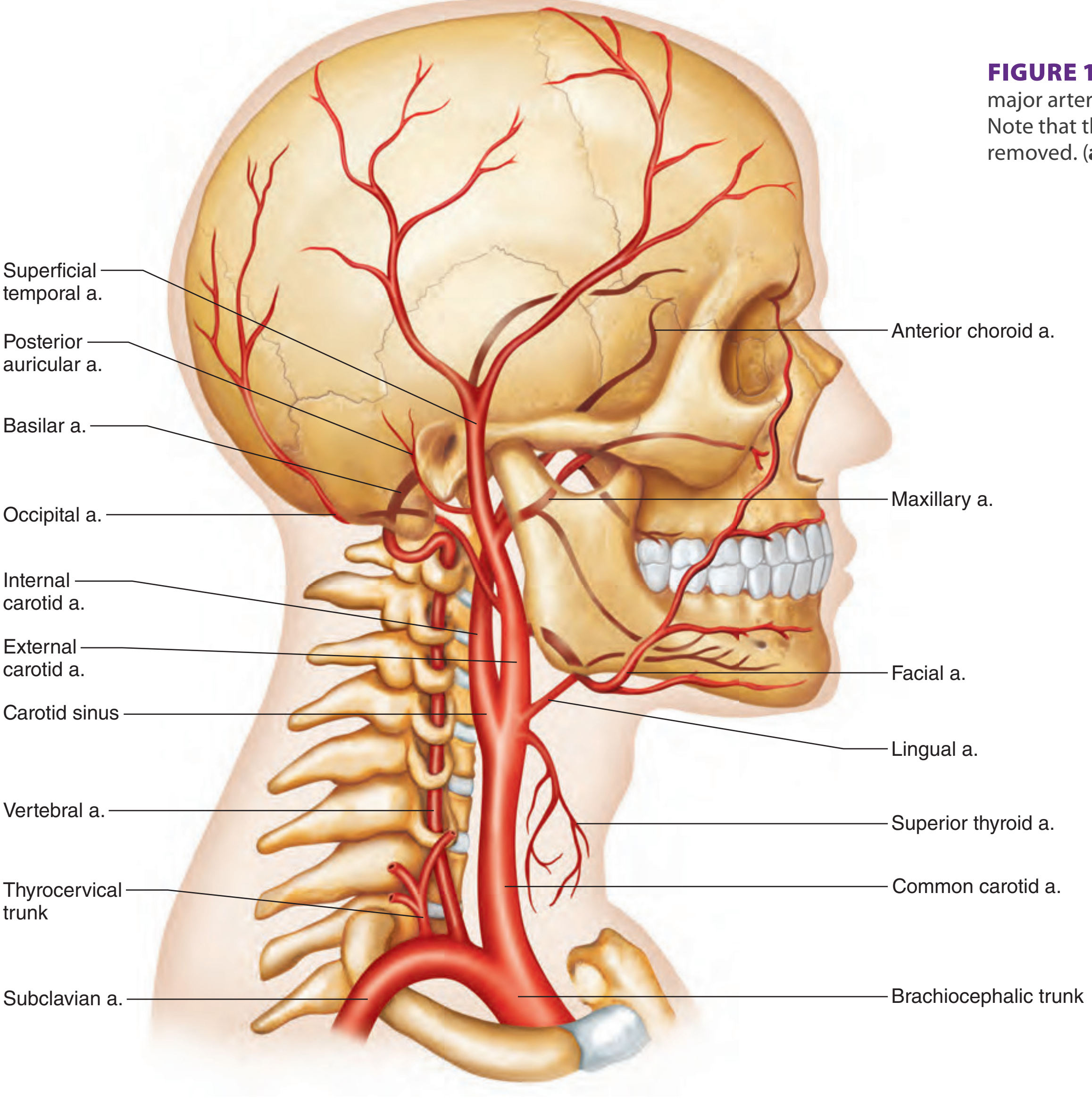

Superficial temporal a.
Posterior auricular a.
Basilar a.
Occipital a.
Internal carotid a.
External carotid a.
Carotid sinus
Vertebral a.
Thyrocervical trunk
Subclavian a.
Anterior choroid a.
Maxillary a.
Facial a.
Lingual a.
Superior thyroid a.
Common carotid a.
Brachiocephalic trunk

**FIGURE 13.28** APR The major arteries of the head and neck. Note that the clavicle has been removed. (**a.** stands for **artery.**)

the **cerebral arterial circle** (circle of Willis) at the base of the brain, which connects the vertebral artery and internal carotid artery systems (fig. 13.29). The union of these systems provides alternate pathways for blood to circumvent blockages and reach brain tissues. It also equalizes blood pressure in the brain's blood supply.

The **thyrocervical** (thi″ro-ser′vĭ-kal) **arteries** are short vessels. At the thyrocervical axis, these vessels give off branches to the thyroid gland, parathyroid glands, larynx, trachea, esophagus, and pharynx, as well as to muscles in the neck, shoulder, and back.

The left and right *common carotid arteries* diverge into the internal and external carotid arteries. The **external carotid artery** courses upward on the side of the head, giving off branches to structures in the neck, face, jaw, scalp, and base of the skull. The **internal carotid artery** follows a deep course upward along the pharynx to the base of the skull. Entering the cranial cavity, it provides the major blood supply to the brain. Near the base of each internal carotid artery is an enlargement called a **carotid sinus.** Like the aortic sinuses, these structures contain baroreceptors that control blood pressure. Table 13.4 summarizes the major branches of the external and internal carotid arteries.

## Arteries to the Shoulder and Upper Limb

The subclavian artery, after branching toward the neck, continues into the arm (fig. 13.30). It passes between the clavicle and the first rib, and becomes the axillary artery. The **axillary artery** supplies branches to structures in the axilla and chest wall and becomes the **brachial artery,** which courses along the humerus to the elbow. It gives rise to a *deep brachial artery* that curves posteriorly around the humerus and supplies the triceps brachii muscle. In the elbow, the brachial artery divides into an ulnar artery and a radial artery.

The **ulnar artery** leads downward on the ulnar side of the forearm to the wrist. Some of its branches supply the elbow joint, and some supply blood to muscles in the forearm.

The **radial artery** extends along the radial side of the forearm to the wrist, supplying the lateral muscles of the forearm. As the radial artery nears the wrist, it

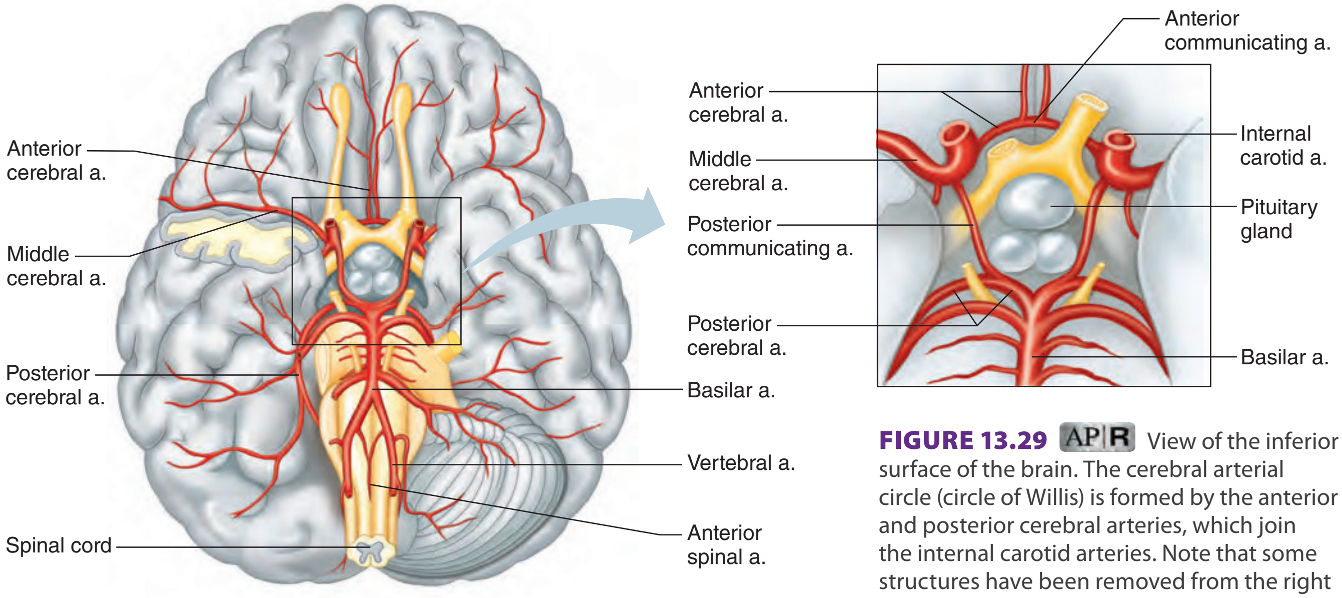


**FIGURE 13.29** APR View of the inferior surface of the brain. The cerebral arterial circle (circle of Willis) is formed by the anterior and posterior cerebral arteries, which join the internal carotid arteries. Note that some structures have been removed from the right side of the figure to show underlying blood vessels. (**a.** stands for **artery.**)

**TABLE 13.4** Major Branches of the External and Internal Carotid Arteries

| Artery | Branch | General Region or Organs Supplied |
|---|---|---|
| External carotid artery | Superior thyroid artery | Larynx and thyroid gland |
| | Lingual artery | Tongue and salivary glands |
| | Facial artery | Pharynx, palate, chin, lips, and nose |
| | Occipital artery | Posterior scalp, meninges, and neck muscles |
| | Posterior auricular artery | Ear and lateral scalp |
| | Maxillary artery | Teeth, jaw, cheek, and eyelids |
| | Superficial temporal artery | Parotid salivary gland and surface of the face and scalp |
| Internal carotid artery | Ophthalmic artery | Eye and eye muscles |
| | Anterior choroid artery | Choroid plexus and brain |
| | Anterior cerebral artery | Frontal and parietal lobes of the brain |

comes close to the surface and provides a convenient vessel for taking the pulse (radial pulse).

At the wrist, the branches of the ulnar and radial arteries join to form a network of vessels. Arteries arising from this network supply blood to the hand.

## Arteries to the Thoracic and Abdominal Walls

Blood reaches the thoracic wall through several vessels. The **internal thoracic artery,** a branch of the subclavian artery, gives off two *anterior intercostal* (in″ter-kos′tal) *arteries* that supply the intercostal muscles and mammary glands. The *posterior intercostal arteries* arise from the thoracic aorta and enter the intercostal spaces. They supply the intercostal muscles, the vertebrae, the spinal cord, and the deep muscles of the back.

Branches of the *internal thoracic* and *external iliac arteries* provide blood to the anterior abdominal wall. Paired vessels originating from the abdominal aorta, including the *phrenic* and *lumbar arteries,* supply blood to structures in the posterior and lateral abdominal wall.

## Arteries to the Pelvis and Lower Limb

The abdominal aorta divides to form the **common iliac** (il′e-ak) **arteries** at the level of the pelvic brim. These vessels provide blood to the pelvic organs, gluteal region, and lower limbs (fig. 13.31). Each common iliac artery divides into an internal and an external branch. The **internal iliac artery** gives off many branches to pelvic muscles and visceral structures, as well as to the gluteal muscles and the external reproductive organs. The **external iliac artery** provides the main blood supply to the lower limbs. It passes downward along the brim of the pelvis and branches to supply the muscles and skin in the lower abdominal wall. Midway between the pubic symphysis and the anterior superior iliac spine of the ilium, the external iliac artery becomes the femoral artery.

The **femoral** (fem′or-al) **artery,** which approaches the anterior surface of the upper thigh, gives off branches to muscles and superficial tissues of the thigh. These branches also supply the skin of the groin and the lower abdominal wall.

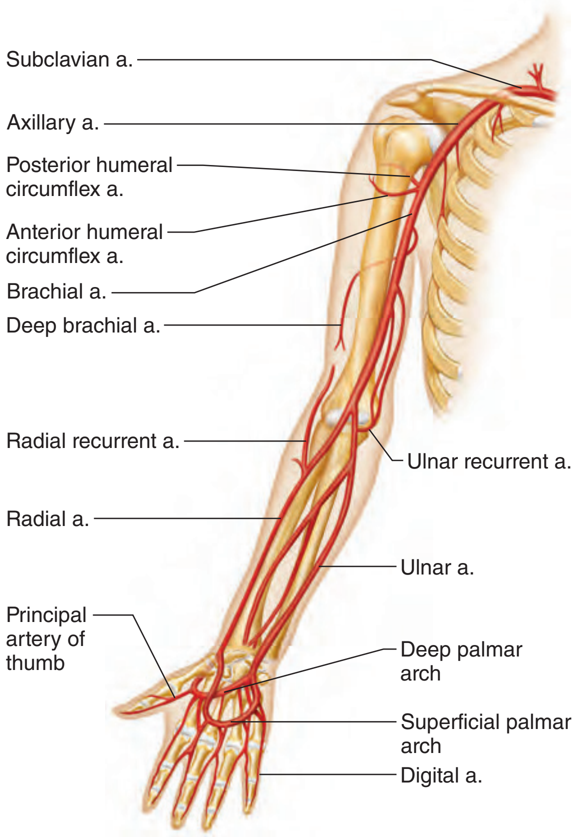


**FIGURE 13.30** APR The major arteries to the shoulder and upper limb. (**a.** stands for **artery.**)

> Q *Blood from the brachial artery flows into which artery (arteries) in the forearm?*
>
> **The answer can be found in Appendix F on page 582.**

As the femoral artery reaches the proximal border of the space behind the knee, it becomes the **popliteal** (pop-lit′e-al) **artery.** Branches of this artery supply blood to the knee joint and to certain muscles in the thigh and calf. The popliteal artery diverges into the anterior and posterior tibial arteries.

The **anterior tibial artery** passes downward between the tibia and fibula, giving off branches to the skin and muscles in the anterior and lateral regions of the leg. This vessel continues into the foot as the *dorsalis pedis artery* (dorsal pedis artery), which supplies blood to the foot. The **posterior tibial artery,** the larger of the two popliteal branches, descends beneath the calf muscles, giving off branches to the skin, muscles, and other tissues of the leg along the way.

### PRACTICE

45. Name the parts of the aorta.
46. Name the vessels that arise from the aortic arch.
47. Name the branches of the thoracic and abdominal aorta.
48. Which vessels supply blood to the head? To the upper limb? To the abdominal wall? To the lower limb?

## 13.8 | Venous System

Venous circulation returns blood to the heart after gases, nutrients, and wastes are exchanged between the blood and body cells.

### Characteristics of Venous Pathways

The vessels of the venous system originate with the merging of the capillaries into venules. Venules then merge into small veins, and small veins meet to form larger ones. Unlike the arterial pathways, however, the vessels of the venous system are difficult to follow because they commonly connect in irregular networks. Many unnamed tributaries may join to form a large vein.

The pathways of larger veins are less variable than those of smaller veins. These veins typically parallel the courses of named arteries, and many bear the same names as their arterial counterparts. For example, the renal vein parallels the renal artery, and the common iliac vein accompanies the common iliac artery.

The veins that carry blood from the lungs and myocardium back to the heart have been described. The veins from all the other parts of the body converge into two major vessels, the **superior** and **inferior venae cavae,** which lead to the right atrium.

### Veins from the Brain, Head, and Neck

The **external jugular** (jug′u-lar) **veins** drain blood from the face, scalp, and superficial regions of the neck. These vessels descend on either side of the neck and empty into the *right* and *left subclavian veins* (fig. 13.32).

The **internal jugular veins,** which are somewhat larger than the external jugular veins, arise from numerous veins and venous sinuses of the brain and from deep veins in parts of the face and neck. They descend through the neck and join the subclavian veins. These unions of the internal jugular and subclavian veins form large **brachiocephalic veins** on each side. These vessels then merge and give rise to the superior vena cava, which enters the right atrium.

### Veins from the Upper Limb and Shoulder

A set of deep veins and a set of superficial veins drain the upper limb. The deep veins generally parallel the arteries in each region and have similar names. Deep venous drainage of the upper limb begins in the digital veins that drain into pairs of **radial veins** and pairs of **ulnar veins**, which empty into a pair of **brachial veins**. The superficial veins connect in complex networks just beneath the skin. They also communicate with the deep vessels of the upper limb, providing many alternate pathways through which blood can leave the tissues (fig. 13.33). The main vessels of the superficial network are the basilic and cephalic veins.

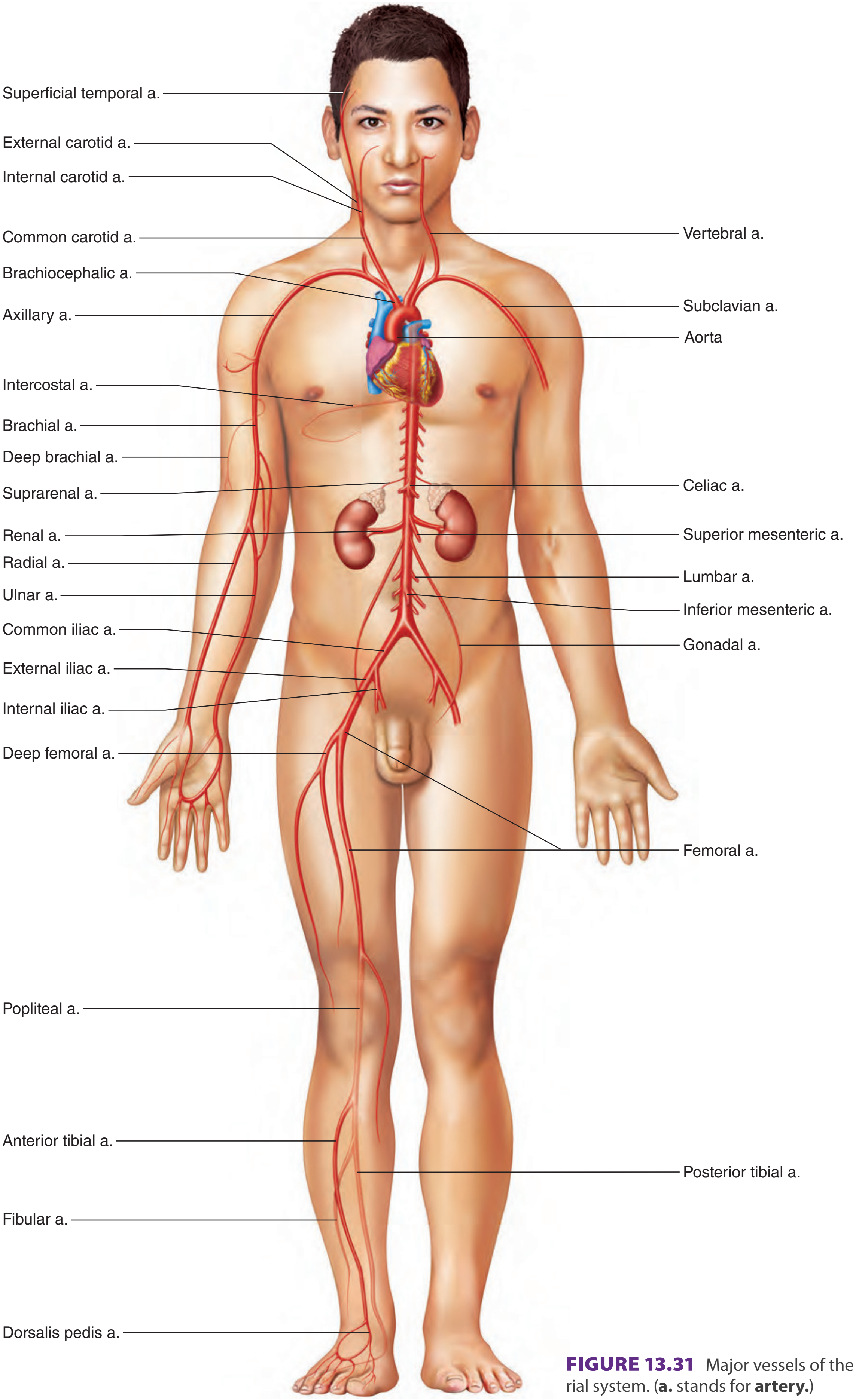

Superficial temporal a.
External carotid a.
Internal carotid a.
Common carotid a.
Brachiocephalic a.
Axillary a.
Intercostal a.
Brachial a.
Deep brachial a.
Suprarenal a.
Renal a.
Radial a.
Ulnar a.
Common iliac a.
External iliac a.
Internal iliac a.
Deep femoral a.
Popliteal a.
Anterior tibial a.
Fibular a.
Dorsalis pedis a.
Vertebral a.
Subclavian a.
Aorta
Celiac a.
Superior mesenteric a.
Lumbar a.
Inferior mesenteric a.
Gonadal a.
Femoral a.
Posterior tibial a.

**FIGURE 13.31** Major vessels of the arterial system. (**a.** stands for **artery.**)

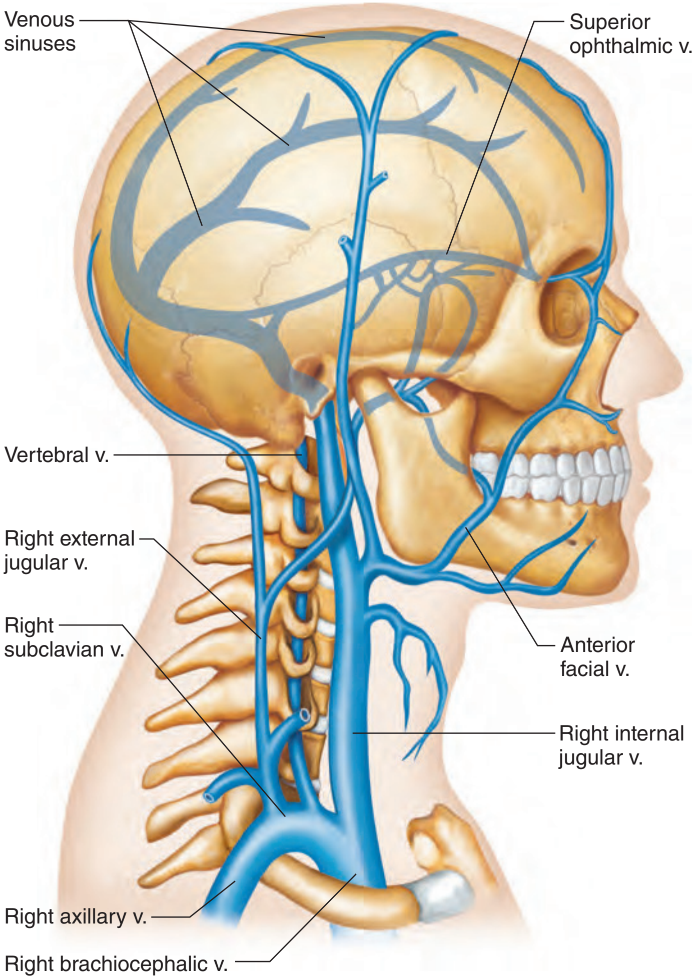

Venous sinuses
Superior ophthalmic v.
Vertebral v.
Right external jugular v.
Right subclavian v.
Anterior facial v.
Right internal jugular v.
Right axillary v.
Right brachiocephalic v.

**FIGURE 13.32** APR The major veins of the brain, head, and neck. Note that the clavicle has been removed. (**v.** stands for **vein.**)

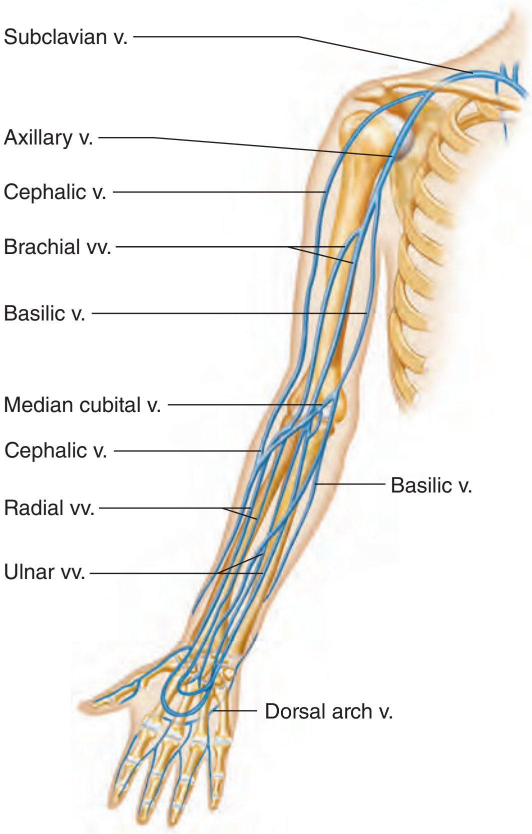

Subclavian v.
Axillary v.
Cephalic v.
Brachial vv.
Basilic v.
Median cubital v.
Cephalic v.
Radial vv.
Ulnar vv.
Basilic v.
Dorsal arch v.

**FIGURE 13.33** APR The major veins of the upper limb and shoulder. (**v.** stands for **vein, vv.** stands for **veins.**)

Q *Blood from the brachial vein and basilic vein drains into which vein(s)?*

**The answer can be found in Appendix F on page 582.**

The **basilic** (bah-sil′ik) **vein** ascends from the forearm to the middle of the arm, where it penetrates deeply and joins the **brachial vein**. The basilic and brachial veins merge, forming the **axillary vein**.

The **cephalic** (sĕ-fal′ik) **vein** courses upward from the hand to the shoulder. In the shoulder, it pierces the tissues and empties into the axillary vein. Beyond the axilla, the axillary vein becomes the subclavian vein.

In the bend of the elbow, a *median cubital vein* ascends from the cephalic vein on the lateral side of the forearm to the basilic vein on the medial side. This large vein is usually visible just beneath the skin. It is often used as a site for *venipuncture,* when it is necessary to remove a blood sample or to add fluids to blood.

## Veins from the Abdominal and Thoracic Walls

Tributaries of the brachiocephalic and azygos veins drain the abdominal and thoracic walls. For example, the **brachiocephalic vein** receives blood from the *internal thoracic vein,* which generally drains the tissues the internal thoracic artery supplies. Some *intercostal veins* also empty into the brachiocephalic vein.

The **azygos** (az′ĭ-gos) **vein** originates in the dorsal abdominal wall and ascends through the mediastinum on the right side of the vertebral column to join the superior vena cava. It drains most of the muscular tissue in the abdominal and thoracic walls.

Tributaries of the azygos vein include the *posterior intercostal veins* on the right side, which drain the intercostal spaces, and the *superior* and *inferior hemiazygos veins,* which receive blood from the posterior intercostal veins on the left. The right and left *ascending lumbar veins,* with tributaries that include vessels from the lumbar and sacral regions, also connect to the azygos system.

## Veins from the Abdominal Viscera

Most veins carry blood directly to the atria of the heart. Veins that drain the abdominal viscera are exceptions (fig. 13.34). They originate in the capillary networks of the stomach, intestines, pancreas, and spleen and carry blood from these organs through a **hepatic portal**

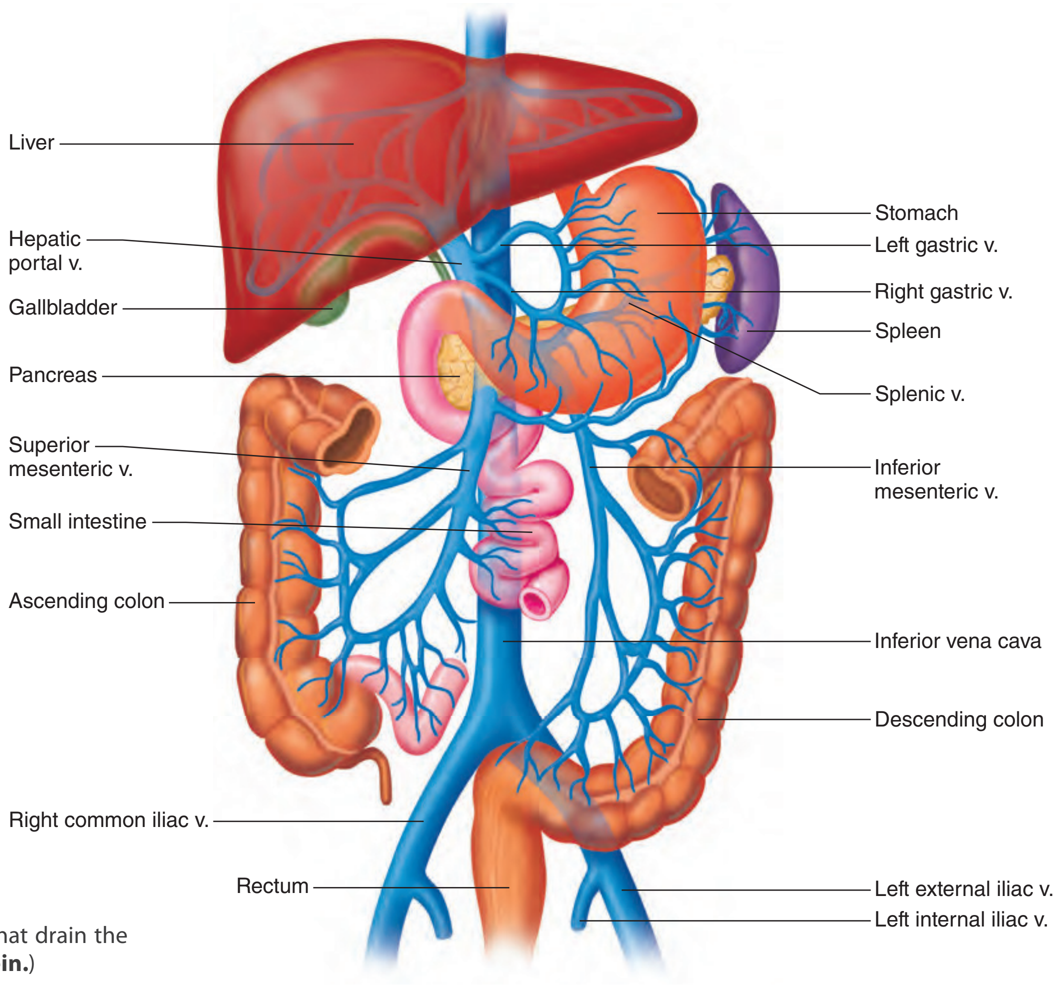


**FIGURE 13.34** APR Veins that drain the abdominal viscera. (**v.** stands for **vein.**)

(por′tal) **vein** to the liver. This unique venous pathway is called the **hepatic portal system.**

Tributaries of the hepatic portal vein include:

1. right and left *gastric veins* from the stomach.
2. *superior mesenteric vein* from the small intestine, ascending colon, and transverse colon.
3. *splenic vein* from a convergence of several veins draining the spleen, the pancreas, and part of the stomach. Its largest tributary, the *inferior mesenteric vein,* brings blood upward from the descending colon, sigmoid colon, and rectum.

About 80% of the blood flowing to the liver in the hepatic portal system comes from capillaries in the stomach and intestines, and is oxygen-poor but nutrient-rich. As discussed in chapter 15 (p. 426), the liver handles these nutrients in a variety of ways. It regulates blood glucose concentration by joining (polymerizing) excess glucose molecules into glycogen for storage, or by breaking down glycogen into glucose when blood glucose concentration drops below normal. The liver helps regulate blood concentrations of recently absorbed amino acids and lipids by modifying them into forms cells can use, by oxidizing them, or by changing them into storage forms. The liver also stores certain vitamins and detoxifies harmful substances. Blood in the hepatic portal vein nearly always contains bacteria that have entered through intestinal capillaries. Large *Kupffer cells* lining small vessels in the liver called hepatic sinusoids phagocytize these microorganisms, removing them from portal blood before it leaves the liver.

After passing through the hepatic sinusoids of the liver, the blood in the hepatic portal system travels through a series of merging vessels into **hepatic veins.** These veins empty into the inferior vena cava, returning the blood to the general circulation.

## Veins from the Lower Limb and Pelvis

Veins that drain blood from the lower limb can be divided into deep and superficial groups, as in the upper limb (fig. 13.35). The deep veins of the leg, such as the *anterior* and *posterior tibial veins,* are named for the arteries they accompany. At the level of the knee, these vessels form a single trunk, the **popliteal vein.** This vein continues upward through the thigh as the **femoral vein,** which in, turn, becomes the **external iliac vein.**

The superficial veins of the foot, leg, and thigh connect to form a complex network beneath the skin. These vessels drain into two major trunks—the small and great saphenous veins. The **small saphenous** (sah-fe′nus) **vein** ascends along the back of the calf, enters the popliteal fossa, and joins the popliteal vein.

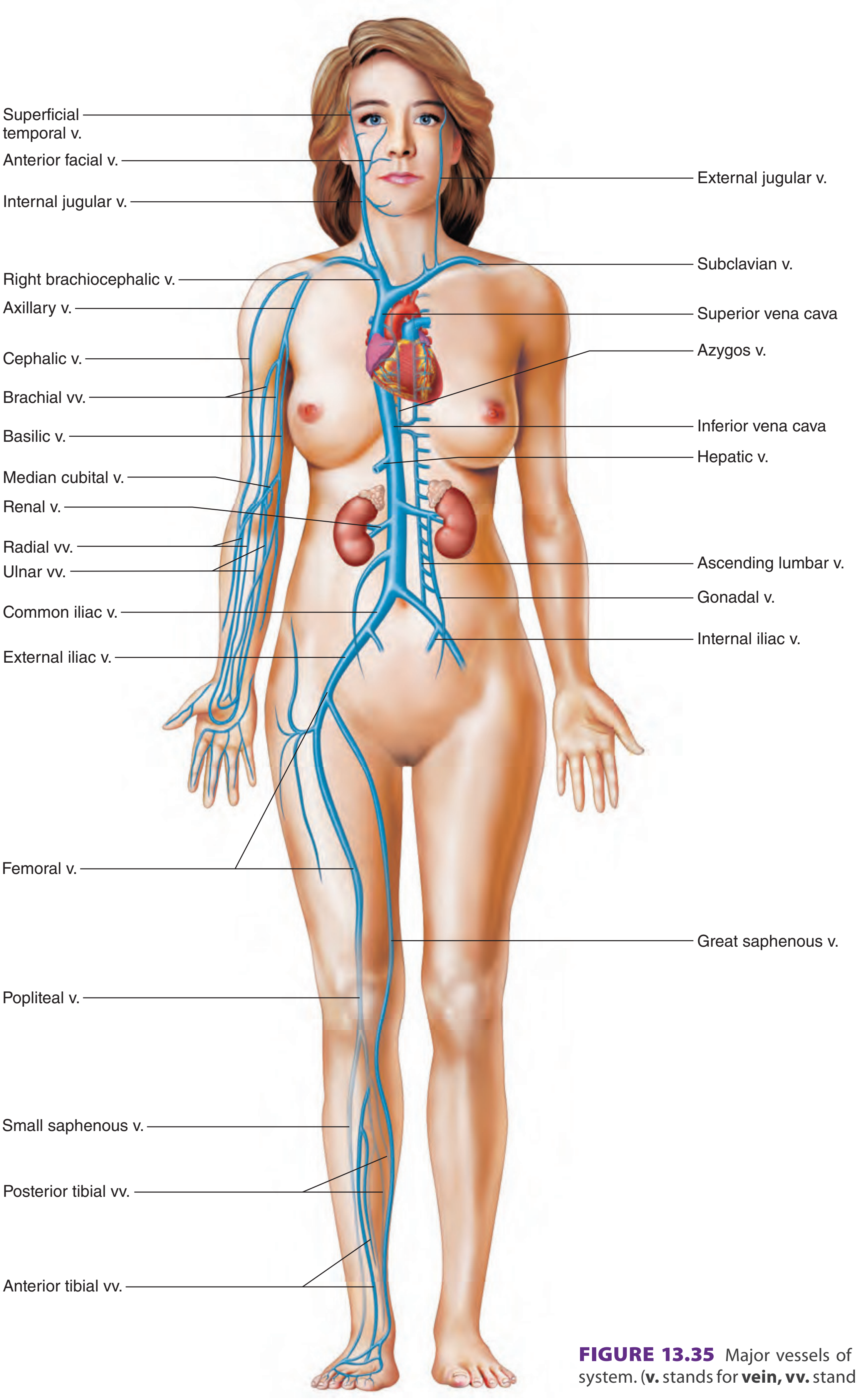

Superficial temporal v.
Anterior facial v.
Internal jugular v.
Right brachiocephalic v.
Axillary v.
Cephalic v.
Brachial vv.
Basilic v.
Median cubital v.
Renal v.
Radial vv.
Ulnar vv.
Common iliac v.
External iliac v.
Femoral v.
Popliteal v.
Small saphenous v.
Posterior tibial vv.
Anterior tibial vv.
External jugular v.
Subclavian v.
Superior vena cava
Azygos v.
Inferior vena cava
Hepatic v.
Ascending lumbar v.
Gonadal v.
Internal iliac v.
Great saphenous v.

**FIGURE 13.35** Major vessels of the venous system. (**v.** stands for **vein, vv.** stands for **veins.**)

The **great saphenous vein,** the longest vein in the body, ascends in front of the medial malleolus and extends upward along the medial side of the leg and thigh. In the thigh, it penetrates deeply and joins the femoral vein. Near its termination, the great saphenous vein receives tributaries from a number of vessels that drain the upper thigh, groin, and lower abdominal wall.

In addition to communicating freely with each other, the saphenous veins communicate extensively with the deep veins of the leg and thigh. Blood can thus return to the heart from the lower extremities by several routes.

In the pelvic region, vessels leading to the **internal iliac vein** carry blood away from the organs of the reproductive, urinary, and digestive systems. The internal iliac veins unite with the right and left external iliac veins to form the **common iliac veins.** These vessels, in turn, merge to produce the inferior vena cava.

**PRACTICE**

49. Name the veins that return blood to the right atrium.
50. Which major veins drain blood from the head? From the upper limbs? From the abdominal viscera? From the lower limbs?

## Summary Outline

### 13.1 Introduction (p. 350)

*The cardiovascular system, consisting of the heart and blood vessels, provides oxygen and nutrients to and removes wastes from body cells.*

### 13.2 Structure of the Heart (p. 350)

1. Size and location of the heart
   a. The heart is about 14 centimeters long and 9 centimeters wide.
   b. It is located within the mediastinum and rests on the diaphragm.
2. Coverings of the heart
   a. A layered pericardium encloses the heart.
   b. The pericardial cavity is a space between the parietal and visceral layers of the pericardium.
3. Wall of the heart
   The wall of the heart has three layers—an epicardium, a myocardium, and an endocardium.
4. Heart chambers and valves
   a. The heart is divided into two atria and two ventricles.
   b. Right chambers and valves
      (1) The right atrium receives blood from the venae cavae and coronary sinus.
      (2) The tricuspid valve separates the right atrium from the right ventricle.
      (3) The right ventricle pumps blood into the pulmonary trunk.
      (4) A pulmonary valve guards the base of the pulmonary trunk.
   c. Left chambers and valves
      (1) The left atrium receives blood from the pulmonary veins.
      (2) The mitral valve separates the left atrium from the left ventricle.
      (3) An aortic valve guards the base of the aorta.
5. Skeleton of the heart
   The skeleton of the heart consists of fibrous rings that enclose the bases of the pulmonary trunk and aorta and masses of dense connective tissues in the septum between the ventricles.
6. Blood flow through the heart
   a. Blood low in oxygen and high in carbon dioxide enters the right side of the heart and is pumped into the pulmonary circulation.
   b. After blood is oxygenated in the lungs and some carbon dioxide is removed, it returns to the left side of the heart through the pulmonary veins.
   c. From the left ventricle, the blood moves into the aorta.
7. Blood supply to the heart
   a. The coronary arteries supply blood to the myocardium.
   b. Blood returns to the right atrium through the cardiac veins and coronary sinus.

### 13.3 Heart Actions (p. 357)

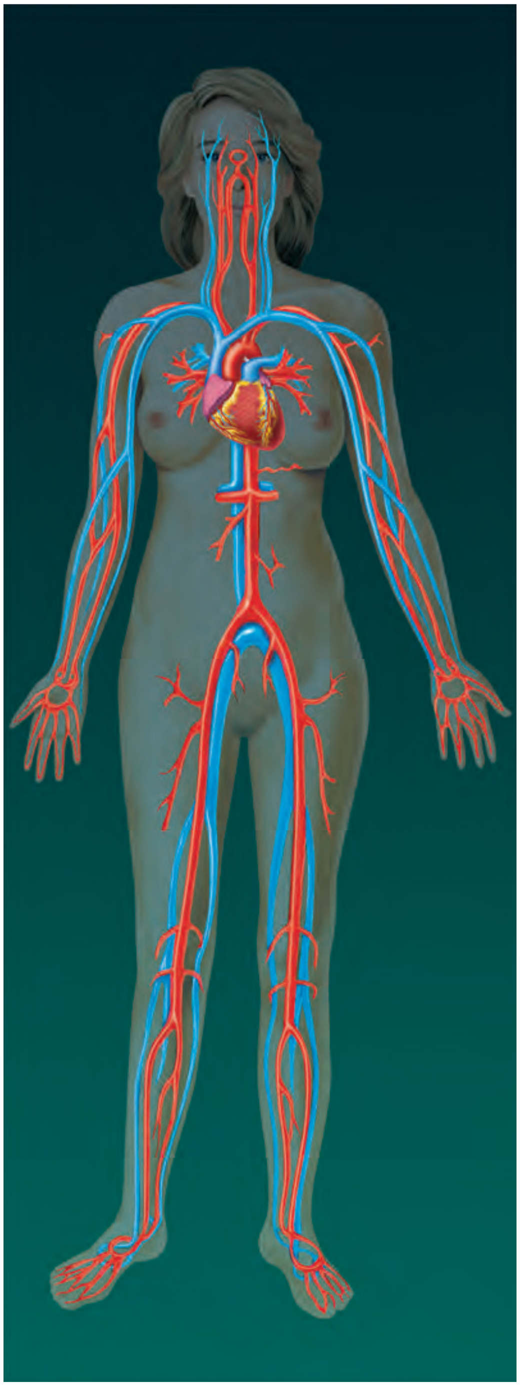
1. Cardiac cycle
   a. The atria contract (atrial systole) while the ventricles relax (ventricular diastole). The ventricles contract (ventricular systole) while the atria relax (atrial diastole).
   b. Pressure within the chambers rises and falls in repeated cycles.
2. Heart sounds
   Heart sounds are due to the vibrations produced when the valves close.
3. Cardiac muscle fibers
   a. Cardiac muscle fibers connect to form a functional syncytium.
   b. If any part of the syncytium is stimulated, the whole structure contracts as a unit.
4. Cardiac conduction system
   a. This system initiates and conducts impulses throughout the myocardium.
   b. Impulses from the SA node pass slowly to the AV node; impulses are conducted rapidly along the AV bundle and Purkinje fibers.
5. Electrocardiogram (ECG)
   a. An ECG records electrical changes in the myocardium during a cardiac cycle.
   b. The pattern contains several waves.
      (1) The P wave represents atrial depolarization.
      (2) The QRS complex represents ventricular depolarization.
      (3) The T wave represents ventricular repolarization.
6. Regulation of the cardiac cycle
   a. Physical exercise, body temperature, and the concentration of various ions affect heart rate.
   b. Branches of sympathetic and parasympathetic nerve fibers innervate the SA and AV nodes.
   c. The cardiac control center in the medulla oblongata regulates autonomic impulses to the heart.

### 13.4 Blood Vessels (p. 363)

*Blood vessels form a closed circuit of tubes that carry blood from the heart to body cells and back again.*

1. Arteries and arterioles
   a. Arteries are adapted to carry blood under relatively high pressure away from the heart.
   b. The walls of arteries and arterioles consist of layers of endothelium, smooth muscle, and connective tissue.
   c. Autonomic fibers innervate smooth muscle in vessel walls, causing vasoconstriction or vasodilation.

# Cardiovascular System



The heart pumps blood through as many as 60,000 miles of blood vessels delivering nutrients to, and removing wastes from, all body cells.

## Integumentary System

Changes in skin blood flow are important in temperature control.

## Lymphatic System

The lymphatic system returns tissue fluids to the bloodstream.

## Skeletal System

Bones help control plasma levels of calcium ions, which influence heart action.

## Digestive System

The digestive system breaks down nutrients into forms readily absorbed by the bloodstream.

## Muscular System

Blood flow increases to exercising skeletal muscle, delivering oxygen and nutrients and removing wastes. Muscle actions help the blood circulate.

## Respiratory System

The respiratory system oxygenates the blood and removes carbon dioxide. Respiratory movements help the blood circulate.

## Nervous System

The brain is especially dependent on blood flow for survival. The nervous system helps control blood flow and blood pressure.

## Urinary System

The kidneys clear the blood of wastes and substances present in the body. The kidneys help control blood pressure and blood volume.

## Endocrine System

Hormones are carried in the bloodstream. Some hormones directly affect the heart and blood vessels.

## Reproductive System

Blood pressure is important in normal function of the sex organs.

2. Capillaries
    a. Capillaries connect arterioles and venules.
    b. The capillary wall is a single layer of cells that forms a semipermeable membrane.
    c. Openings in capillary walls, where endothelial cells overlap, vary in size from tissue to tissue.
    d. Precapillary sphincters regulate capillary blood flow.
    e. Capillary blood and tissue fluid exchange gases, nutrients, and metabolic by-products.
        (1) Diffusion provides the most important means of transport.
        (2) Filtration, due to the hydrostatic pressure of blood, causes a net outward movement of fluid at the arteriolar end of a capillary.
        (3) Osmosis due to colloid osmotic pressure causes a net inward movement of fluid at the venular end of a capillary.
3. Venules and veins
    a. Venules continue from capillaries and merge to form veins.
    b. Veins carry blood to the heart.
    c. Venous walls are similar to arterial walls, but are thinner and contain less smooth muscle and elastic tissue.

### 13.5 Blood Pressure (p. 369)

*Blood pressure is the force blood exerts against the inner walls of blood vessels.*

1. Arterial blood pressure
    a. Arterial blood pressure rises and falls with the phases of the cardiac cycle.
    b. Systolic pressure occurs when the ventricle contracts; diastolic pressure occurs when the ventricle relaxes.
2. Factors that influence arterial blood pressure
   Arterial blood pressure increases as cardiac output, blood volume, peripheral resistance, or blood viscosity increases.
3. Control of blood pressure
    a. Blood pressure is controlled in part by the mechanisms that regulate cardiac output and peripheral resistance.
    b. The more blood that enters the heart, the stronger the ventricular contraction, the greater the stroke volume, and the greater the cardiac output.
    c. The baroreceptor reflexes involving the cardiac control center of the medulla oblongata regulate heart rate.
4. Venous blood flow
    a. Venous blood flow depends on skeletal muscle contraction, breathing movements, and venoconstriction.
    b. Many veins contain flaplike valves that prevent blood from backing up.

### 13.6 Paths of Circulation (p. 373)

1. Pulmonary circuit
   The pulmonary circuit consists of vessels that carry blood from the right ventricle to the lungs and back to the left atrium.
2. Systemic circuit
    a. The systemic circuit consists of vessels that lead from the left ventricle to the body cells (including those of the heart itself) and back to the heart.
    b. It includes the aorta and its branches, as well as the system of veins that return blood to the right atrium.

### 13.7 Arterial System (p. 373)

1. Principal branches of the aorta
    a. The aorta is the largest artery with respect to diameter.
    b. The branches of the ascending aorta include the right and left coronary arteries.
    c. The branches of the aortic arch include the brachiocephalic, left common carotid, and left subclavian arteries.
    d. The branches of the descending aorta include the thoracic and abdominal groups.
    e. The abdominal aorta diverges into the right and left common iliac arteries.
2. Arteries to the neck, head, and brain
   These include branches of the subclavian and common carotid arteries.
3. Arteries to the shoulder and upper limb
    a. The subclavian artery passes into the upper limb, and in various regions is called the axillary and brachial artery.
    b. Branches of the brachial artery include the ulnar and radial arteries.
4. Arteries to the thoracic and abdominal walls
    a. Branches of the subclavian artery and thoracic aorta supply the thoracic wall.
    b. Branches of the abdominal aorta and other arteries supply the abdominal wall.
5. Arteries to the pelvis and lower limb
   The common iliac arteries supply the pelvic organs, gluteal region, and lower limbs.

### 13.8 Venous System (p. 377)

1. Characteristics of venous pathways
    a. Veins return blood to the heart.
    b. Larger veins usually parallel the paths of major arteries.
2. Veins from the brain, head, and neck
    a. Jugular veins drain these regions.
    b. Jugular veins unite with subclavian veins to form the brachiocephalic veins.
3. Veins from the upper limb and shoulder
    a. Sets of superficial and deep veins drain these regions.
    b. Deep veins parallel arteries with similar names.
4. Veins from the abdominal and thoracic walls
   Tributaries of the brachiocephalic and azygos veins drain these walls.
5. Veins from the abdominal viscera
    a. Blood from the abdominal viscera enters the hepatic portal system and is carried to the liver.
    b. From the liver, hepatic veins carry blood to the inferior vena cava.
6. Veins from the lower limb and pelvis
    a. Sets of deep and superficial veins drain these regions.
    b. The deep veins include the tibial veins, and the superficial veins include the saphenous veins.

## CHAPTER ASSESSMENTS

### 13.1 Introduction

**1.** The cardiovascular system includes ____________. (p. 350)
   a. the heart
   b. the arteries and veins
   c. the capillaries
   d. all of the above

### 13.2 Structure of the Heart

**2.** Describe the pericardium. (p. 351)
**3.** Compare the layers of the heart wall. (p. 352)
**4.** Draw a heart and label the chambers and valves. (pp. 352–353)

5. Blood flows through the vena cavae and coronary sinus into the right atrium through the __________ to the right ventricle, through the pulmonary valve to the pulmonary trunk into the right and left __________ to the lungs, then leaves the lungs through the pulmonary veins and flows into the __________ , through the mitral valve to the __________ , and through the __________ to the aorta. (pp. 354–356)
6. List the vessels through which blood flows from the aorta to the myocardium and back to the right atrium (p. 357)

### 13.3 Heart Actions

7. Describe the pressure changes in the atria and ventricles during a cardiac cycle. (p. 357)
8. Distinguish between the roles of the SA node and the AV node. (p. 360)
9. Explain how the cardiac conduction system controls the cardiac cycle. (p. 360)
10. Describe and explain the normal ECG pattern. (p. 361)
11. Discuss how the nervous system regulates the cardiac cycle. (p. 362)

### 13.4 Blood Vessels

12. Distinguish between an artery and an arteriole. (p. 364)
13. Explain control of vasoconstriction and vasodilation. (pp. 364 and 366)
14. Describe the structure and function of a capillary. (p. 366)
15. Relate how diffusion functions in the exchange of substances between the blood and tissues. (p. 367)
16. Explain why water and dissolved substances leave the arteriolar end of a capillary and enter the venular end. (p. 367)
17. Distinguish between a vein and a venule. (p. 367)

### 13.5 Blood Pressure

18. Arterial blood pressure peaks when the ventricles contract. This maximum pressure achieved is called __________. (p. 369)
19. Name several factors that influence blood pressure, and explain how each produces its effect. (p. 370)
20. Describe the control of blood pressure. (pp. 370–371)
21. Which of the following promote the flow of venous blood? (p. 372)
    a. skeletal muscle contraction
    b. breathing
    c. venoconstriction
    d. all of the above

### 13.6 Paths of Circulation

22. Distinguish between the pulmonary and systemic circuits of the cardiovascular system. (p. 373)

### 13.7–13.8 Arterial System–Venous System

23. Describe the aorta, and name its principal branches. (p. 373)
24. Discuss the relationship between the major venous pathways and the major arterial pathways to the head, upper limbs, abdominal viscera, and lower limbs. (p. 377)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 5.2, 5.3, 13.4

1. If you were asked to invent a blood vessel (artery, capillary, or vein) substitute, what materials might you use to build it? Include synthetic as well as natural materials.

### OUTCOMES 5.5, 9.16, 13.2, 13.3

2. What structures and properties should an artificial heart have?

### OUTCOMES 13.2, 13.4, 13.6, 13.7. 13.8

3. If a patient develops a blood clot in the femoral vein of the left lower limb and a portion of the clot breaks loose, where is the blood flow likely to carry the embolus? What symptoms are likely?

### OUTCOMES 13.2, 13.7

4. If a cardiologist inserts a catheter into a patient's right femoral artery, which arteries will the tube have to pass through in order to reach the entrance to the left coronary artery?

### OUTCOMES 13.4, 13.5, 13.8

5. Cirrhosis of the liver, a disease commonly associated with alcoholism, obstructs blood flow through hepatic blood vessels. As a result, blood backs up and capillary pressure greatly increases in organs drained by the hepatic portal system. What effects might this increasing capillary pressure produce, and which organs would it affect?

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# 14

# Lymphatic System and Immunity

*Peculiarities of peanuts, combined with our fondness for them, sets the stage for allergy, a misdirected immune reaction.*

Peanut allergy. The young woman went to the emergency department for sudden onset of difficulty breathing. She was also flushed and had vomited. An astute medical student taking a quick history from the woman's roommates discovered that she had just eaten cookies from a vending machine in their dorm. Suspecting that the cookies may have contained peanuts, the medical student alerted the attending physician, who treated the woman for suspected peanut allergy—giving oxygen, an antihistamine, a steroid drug, and epinephrine. She recovered.

Peanut allergy is common and on the rise in certain countries. In the United States, 1% of children under the age of five and 2% of the population over ten years of age have had allergic reactions to peanuts. About 30,000 people react each year, and about 200 die. In Denmark and Norway, where peanuts are rarely eaten, peanut allergy is very uncommon.

Peculiarities of peanuts and our fondness for them may explain why peanut allergy prevalence is increasing. Certain glycoproteins in peanuts are allergens, causing the misdirected immune response that is an allergy. These glycoproteins are highly concentrated in the peanut and are resistant to digestion. When eaten they disturb the intestinal lining in such a way that they enter the circulation rapidly. Many allergens encounter cells of the immune system beneath the intestinal lining.

Another factor in the increased incidence of peanut allergy is that people in the United States eat many peanuts. Virtually everyone has eaten a peanut by two years of age, usually in peanut butter. This is sufficient exposure to set the stage for later allergy in genetically predisposed individuals. The young average age of first allergic reaction to peanuts—fourteen months—suggests that the initial exposure necessary to "prime" the immune system for future allergic response may happen through breast milk or in the uterus.

The dry roasting of peanuts in the United States may make the three glycoproteins that evoke the allergic response more active. In China, where peanuts are equally popular but are eaten boiled or fried, allergy is rare. However, children of Chinese immigrants in the United States have the same incidence of peanut allergy as other children in the United States, supporting the idea that method of preparation may contribute to allergenicity.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 14.1 Introduction

**1.** Describe the general functions of the lymphatic system. (p. 387)

### 14.2 Lymphatic Pathways

**2.** Identify the locations of the major lymphatic pathways. (p. 388)

### 14.3 Tissue Fluid and Lymph

**3.** Describe how tissue fluid and lymph form, and explain the function of lymph. (p. 389)

### 14.4 Lymph Movement

**4.** Explain how lymphatic circulation is maintained. (p. 390)

Anatomy & Physiology REVEALED aprevealed.com **Module 10** Lymphatic System

**14.5 Lymphatic Tissues and Lymphatic Organs**

**5.** Describe a lymph node and its major functions. (p. 391)
**6.** Discuss the locations and functions of the thymus and spleen. (p. 392)

**14.6 Body Defenses Against Infection**

**7.** Distinguish between innate (nonspecific) and adaptive (specific) defenses. (p. 394)

**14.7 Innate (Nonspecific) Defenses**

**8.** List seven innate body defense mechanisms, and describe the action of each mechanism. (pp. 394–395)

**14.8 Adaptive (Specific) Defenses, or Immunity**

**9.** Explain how two major types of lymphocytes are formed and activated, and how they function in immune mechanisms. (pp. 396–400)
**10.** Discuss the actions of the five types of antibodies. (p. 401)
**11.** Distinguish between primary and secondary immune responses. (p. 402)
**12.** Distinguish between active and passive immunity. (p. 402)
**13.** Explain how allergic reactions, tissue rejection reactions, and autoimmunity arise from immune mechanisms. (pp. 403–404)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**-gen** [be produced] aller*gen*: Substance that evokes an allergic response.

**humor-** [fluid] *humor*al immunity: Immunity resulting from antibodies in body fluids.

**immun-** [free] *immun*ity: Resistance to (freedom from) a specific disease.

**inflamm-** [set on fire] *inflamm*ation: Localized redness, heat, swelling, and pain in tissues.

**nod-** [knot] *nod*ule: Small mass of lymphocytes surrounded by connective tissue.

**patho-** [disease] *patho*gen: Disease-causing agent.

---

## 14.1 | Introduction

The **lymphatic** (lim-fat′ik) **system** is a vast collection of cells and biochemicals that travel in lymphatic vessels, and the organs and glands that produce them. The lymphatic system includes a network of vessels that assist in circulating body fluids, so it is closely associated with the cardiovascular system. Lymphatic vessels transport excess fluid away from interstitial spaces in most tissues and return it to the bloodstream (fig. 14.1). Without the lymphatic system, this fluid would accumulate in tissue spaces. Special lymphatic capillaries, called *lacteals* (lak′te-alz), are located in the lining of the small intestine, where they absorb digested fats and transport them to the venous circulation.

The lymphatic system has a second major function—it enables us to live in a world with different types of organisms, some of which take up residence in or on the human body and may cause infectious diseases. Cells and biochemicals of the lymphatic system launch both generalized and targeted attacks against "foreign" particles, enabling the body to destroy infectious agents. This immunity against disease also protects against toxins and cancer cells. When the immune response is abnormal, persistent infection, cancer, allergies, and autoimmune disorders may result.

### PRACTICE

1. What are the general functions of the lymphatic system?

---

CAREER CORNER

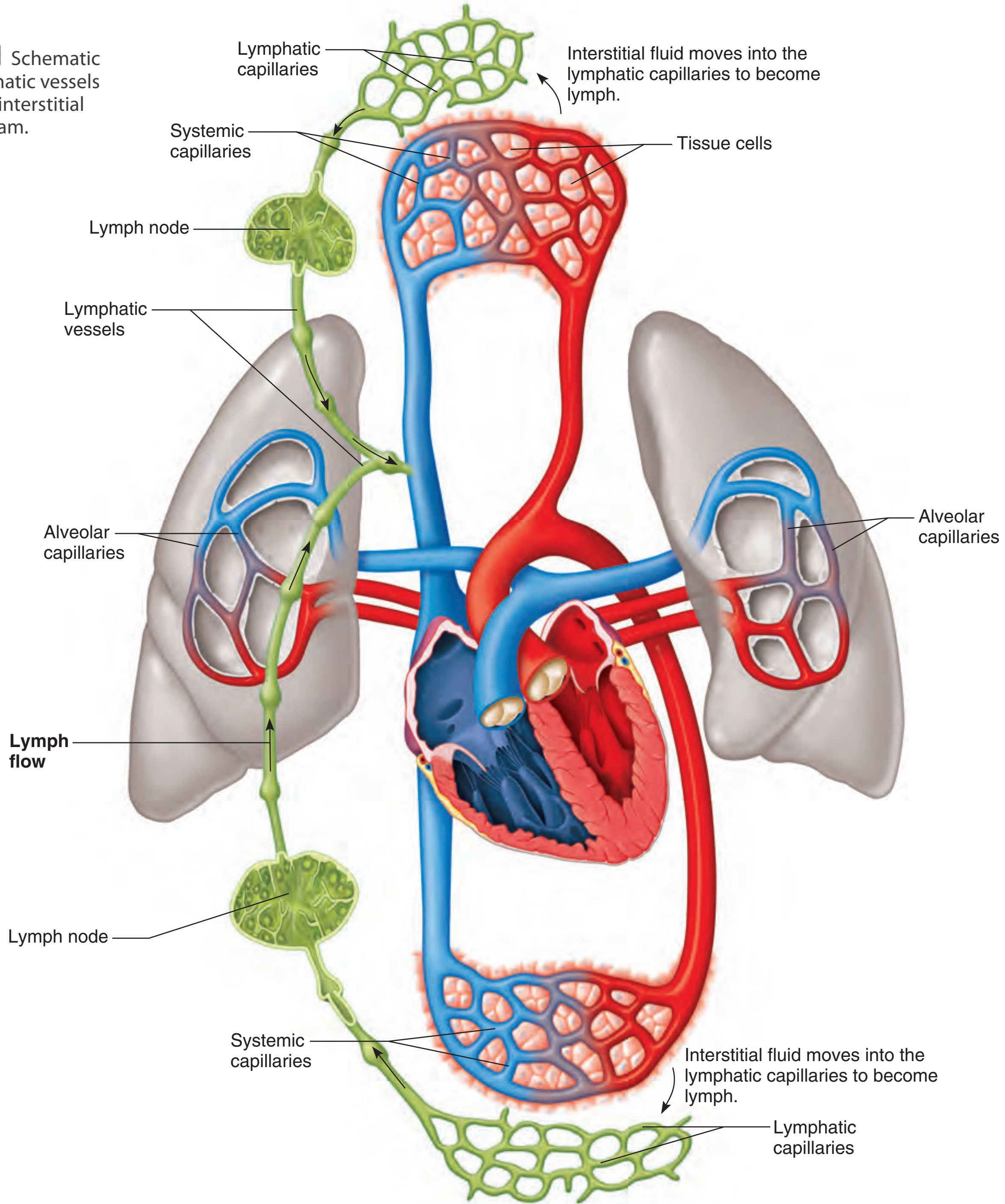
### Public Health Nurse

A hurricane unexpectedly veers inland and churns up rivers, flooding several towns. Residents are evacuated. When the residents return weeks later, public health nurses go door-to-door, warning people about the dangers of exposure to respiratory irritants such as mold and assisting them with getting help.

Public health nurses work in a variety of settings. They vaccinate children in schools, talk to senior citizens about coping with chronic illness or physical limitations, educate parents of preschoolers about avoiding or treating scalp lice, and conduct blood pressure screenings at shopping malls. These health-care professionals are particularly valuable in underserved communities, where they educate the public and help them to access health-care services.

A public health nurse is a registered nurse with specialized training in community-based care. Training includes courses in public policy, health administration, and public health. It is very helpful for a public health nurse to speak the primary languages of the communities served (for instance, bilingual in English and Spanish). Volunteer work at the community level is a good way to prepare for this career. A public health nurse must be able to work well with groups. Employment requires passing a national licensing exam.

**FIGURE 14.1** APR Schematic representation of lymphatic vessels transporting fluid from interstitial spaces to the bloodstream.


Lymphatic capillaries
Interstitial fluid moves into the lymphatic capillaries to become lymph.
Systemic capillaries
Tissue cells
Lymph node
Lymphatic vessels
Alveolar capillaries
Alveolar capillaries
Lymph flow
Lymph node
Systemic capillaries
Interstitial fluid moves into the lymphatic capillaries to become lymph.
Lymphatic capillaries

## 14.2 | Lymphatic Pathways

The **lymphatic pathways** begin as lymphatic capillaries. These tiny tubes merge to form larger lymphatic vessels, which in turn lead to larger vessels that unite with the veins in the thorax.

### Lymphatic Capillaries

**Lymphatic capillaries** are microscopic, closed-ended tubes (fig. 14.2). They extend into interstitial spaces, forming complex networks that parallel the networks of the blood capillaries. Lymph capillaries are nearly everywhere there are blood capillaries, except in the central nervous system. The walls of lymphatic capillaries, like those of blood capillaries, are formed from a single layer of squamous epithelial cells. These thin walls allow tissue fluid (interstitial fluid) to enter lymphatic capillaries. Once inside lymphatic capillaries the fluid is called **lymph** (limf).

### Lymphatic Vessels

The walls of **lymphatic vessels** are similar to those of veins, but are thinner. Like some peripheral veins, lymphatic vessels have flaplike valves which help prevent backflow of lymph (fig. 14.3).

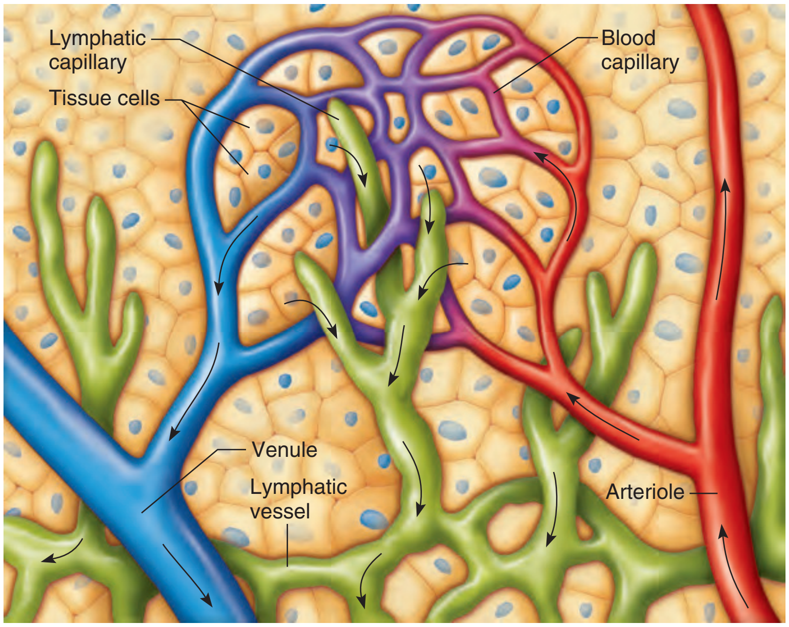


**FIGURE 14.2** Lymphatic capillaries are microscopic, closed-ended tubes that originate in the interstitial spaces of most tissues.

The larger lymphatic vessels lead to specialized organs called **lymph nodes** (limf nōdz). After leaving the nodes, the vessels merge to form still larger lymphatic trunks.

## Lymphatic Trunks and Collecting Ducts

**Lymphatic trunks,** which drain lymph from the lymphatic vessels, are named for the regions they serve. They join one of two **collecting ducts**—the thoracic duct or the right lymphatic duct (fig. 14.4*a*).

The **thoracic duct** is the wider and longer collecting duct. It receives lymph from the lower limbs and abdominal regions, left upper limb, and left side of the thorax, head, and neck, and empties into the left subclavian vein near the junction of the left jugular vein. The **right lymphatic duct** receives lymph from the right side of the head and neck, right upper limb, and right thorax, and empties into the right subclavian vein near the junction of the right jugular vein.

After leaving the two collecting ducts, lymph enters the venous system and becomes part of the plasma just before blood returns to the right atrium. Figure 14.5 summarizes the typical lymphatic pathway.

**PRACTICE**

2. Distinguish between the thoracic duct and the right lymphatic duct.

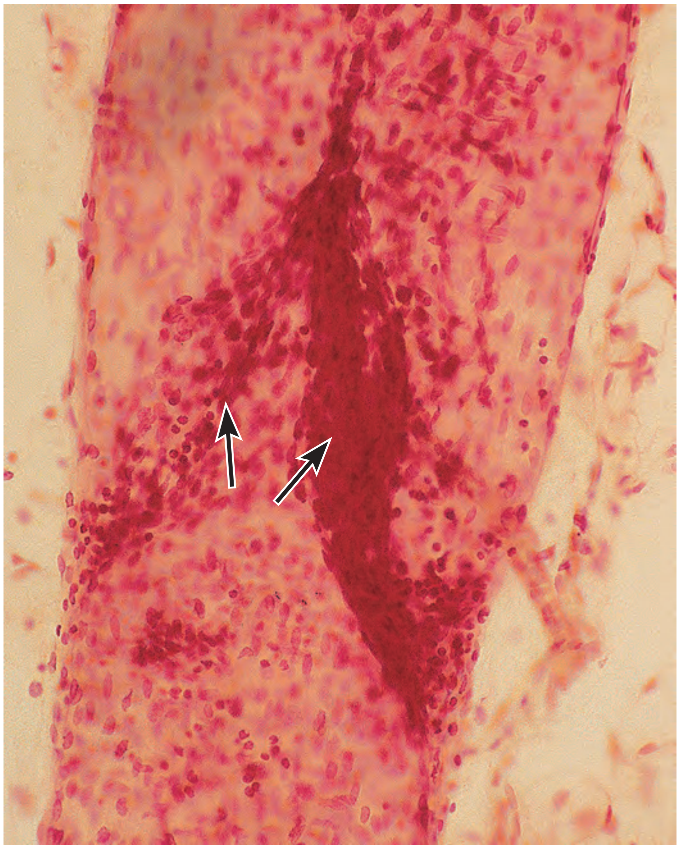


**FIGURE 14.3** Light micrograph of the flaplike valve (arrows) within a lymphatic vessel (60×).

## 14.3 | Tissue Fluid and Lymph

Lymph is essentially tissue fluid that has entered a lymphatic capillary. Thus, lymph formation depends upon tissue fluid formation.

### Tissue Fluid Formation

Recall from chapter 13 (p. 367) that tissue fluid originates from blood plasma. It is composed of water and dissolved substances that leave blood capillaries by filtration as capillary blood pressure forces water and small molecules from the plasma. The resulting fluid is very similar in composition to the blood plasma (including nutrients, gases, and hormones), with the important exception of the plasma proteins, which are generally too large to pass through the capillary walls. The osmotic effect of these proteins (called the *plasma colloid osmotic pressure*) helps draw fluid back into the capillaries by osmosis.

### Lymph Formation and Function

Filtration from the plasma normally exceeds reabsorption, leading to the net formation of tissue fluid. This increases the tissue fluid hydrostatic pressure, which moves tissue

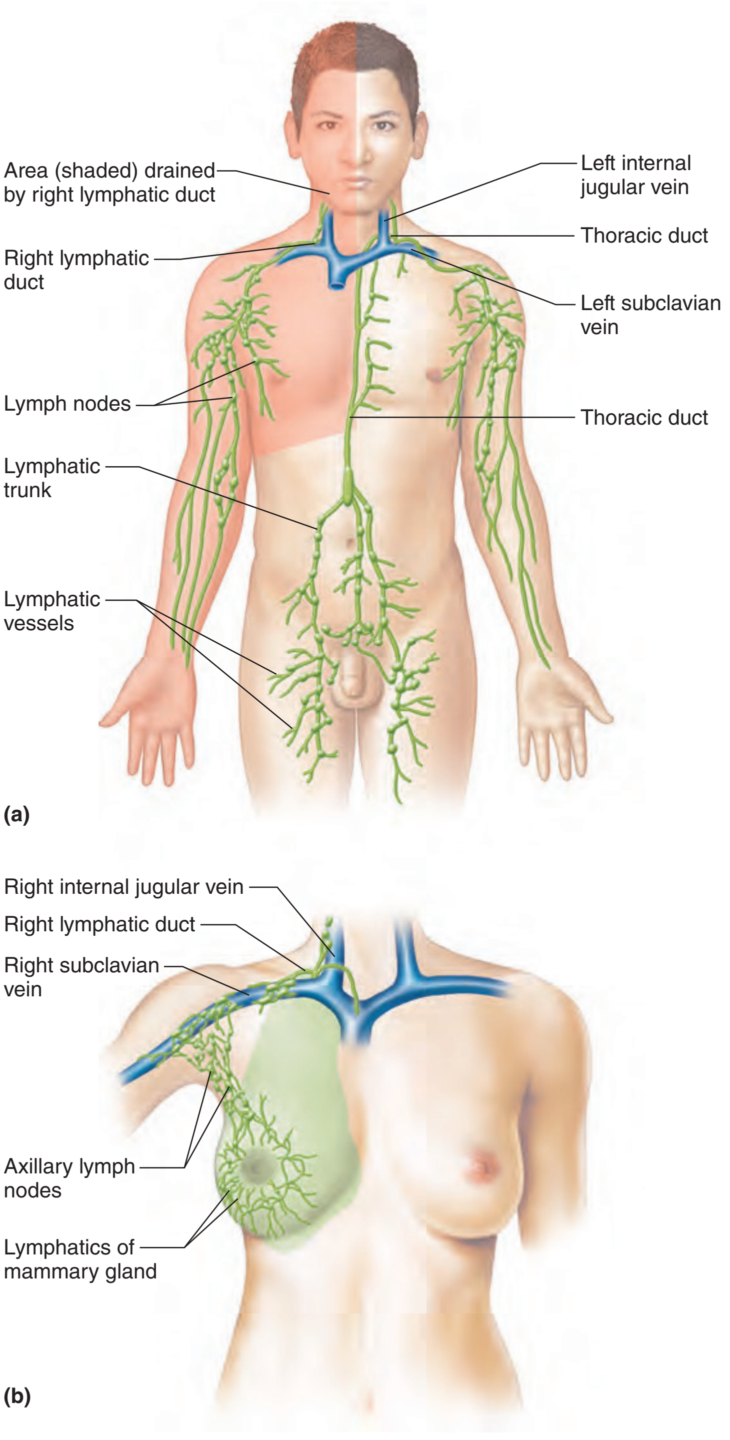

Area (shaded) drained by right lymphatic duct
Right lymphatic duct
Lymph nodes
Lymphatic trunk
Lymphatic vessels
Left internal jugular vein
Thoracic duct
Left subclavian vein
Thoracic duct
(a)
Right internal jugular vein
Right lymphatic duct
Right subclavian vein
Axillary lymph nodes
Lymphatics of mammary gland
(b)

**FIGURE 14.4** APR Lymphatic pathways. **(a)** The right lymphatic duct drains lymph from the upper right side of the body, whereas the thoracic duct drains lymph from the rest of the body. **(b)** Lymph drainage of the right breast illustrates a localized function of the lymphatic system. Surgery to treat breast cancer can disrupt this drainage, causing painful swelling (edema) in the upper limb of the treated side.

Q *Which lymphatic duct drains lymph from the right lower limb?*

**Answer can be found in Appendix F on page 582.**

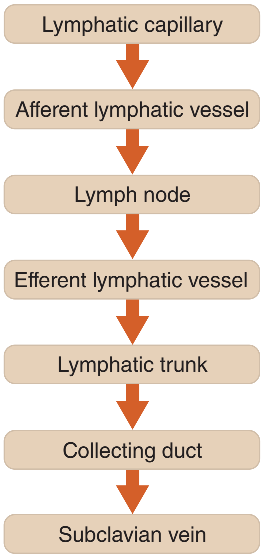

Lymphatic capillary
Afferent lymphatic vessel
Lymph node
Efferent lymphatic vessel
Lymphatic trunk
Collecting duct
Subclavian vein

**FIGURE 14.5** The lymphatic pathway.

fluid into lymphatic capillaries, forming lymph (see fig. 14.2). Lymph returns to the bloodstream most of the small proteins that the blood capillaries filtered. At the same time, lymph transports foreign particles, such as bacteria and viruses, to lymph nodes.

## PRACTICE

3. What is the relationship between tissue fluid and lymph?
4. How do plasma proteins in tissue fluid affect lymph formation?
5. What are the major functions of lymph?

## 14.4 | Lymph Movement

The hydrostatic pressure of tissue fluid drives lymph into lymphatic capillaries. However, muscular activity largely influences the movement of lymph through the lymphatic vessels. Lymph, like venous blood, is under relatively low hydrostatic pressure and may not flow readily through the lymphatic vessels without help from contraction of skeletal muscles in the limbs, contraction of the smooth muscle in the walls of the larger lymphatic trunks, and pressure changes associated with breathing.

Contracting skeletal muscles compress lymphatic vessels. This squeezing action moves the lymph inside lymphatic vessels. Valves in these vessels prevent backflow, so lymph can only move toward a collecting duct. Additionally, smooth muscle in the walls of larger lymphatic trunks contracts rhythmically and compresses the lymph inside, forcing the fluid onward.

Breathing aids lymph circulation by creating a relatively low pressure in the thoracic cavity during inhalation. At the same time, the contracting diaphragm increases the pressure in the abdominal cavity. Consequently, lymph is squeezed out of the abdominal vessels and forced into the thoracic vessels. Once again, valves in lymphatic vessels prevent lymph backflow.

The continuous movement of fluid from interstitial spaces into blood and lymphatic capillaries stabilizes the volume of fluid in these interstitial spaces. Conditions that interfere with lymph movement cause tissue fluid to accumulate within the interstitial spaces, producing *edema* (ĕ-de′mah), or swelling. Edema may develop when surgery removes lymphatic tissue, preventing lymph flow. For example, a surgeon removing a cancerous breast tumor may also remove nearby axillary lymph nodes to prevent associated lymphatic vessels from transporting cancer cells to other sites. Removing this lymphatic tissue can obstruct drainage from the upper limb, causing edema (see fig. 14.4*b*).

## PRACTICE

6. What factors promote lymph flow?
7. What is the consequence of lymphatic obstruction?

## 14.5 Lymphatic Tissues and Lymphatic Organs

Lymphatic tissue contains lymphocytes, macrophages, and other cells. The lymphatic tissue associated with the digestive, respiratory, urinary, and reproductive tracts is called the mucosa-associated lymphoid tissue (MALT). This part of the lymphatic system is diffuse and unencapsulated. Compact masses of lymphatic tissue called **lymph nodules** compose the tonsils and appendix (see chapter 15, pp. 415 and 436). Aggregates of lymph nodules, called *Peyer's patches*, are scattered throughout the mucosal lining of the distal portion of the small intestine. The lymphatic organs, including the lymph nodes, thymus, and spleen, are encapsulated lymphatic tissue.

### Lymph Nodes

Lymph nodes vary in size and shape, but are usually less than 2.5 centimeters long and somewhat bean-shaped (figs. 14.6 and 14.7). Blood vessels and nerves join a lymph node through the indented region of the node, called the **hilum.** The lymphatic vessels leading to a node (afferent vessels) enter separately at various points on its convex surface, but the lymphatic vessels leaving the node (efferent vessels) exit from the hilum.

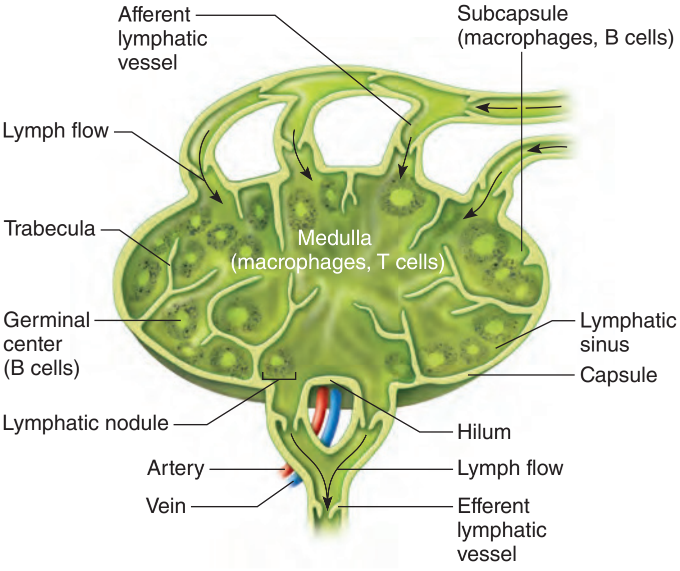

Afferent lymphatic vessel
Subcapsule (macrophages, B cells)
Lymph flow
Trabecula
Medulla (macrophages, T cells)
Germinal center (B cells)
Lymphatic sinus
Capsule
Lymphatic nodule
Hilum
Artery
Lymph flow
Vein
Efferent lymphatic vessel

**FIGURE 14.6** APR A section through a lymph node.

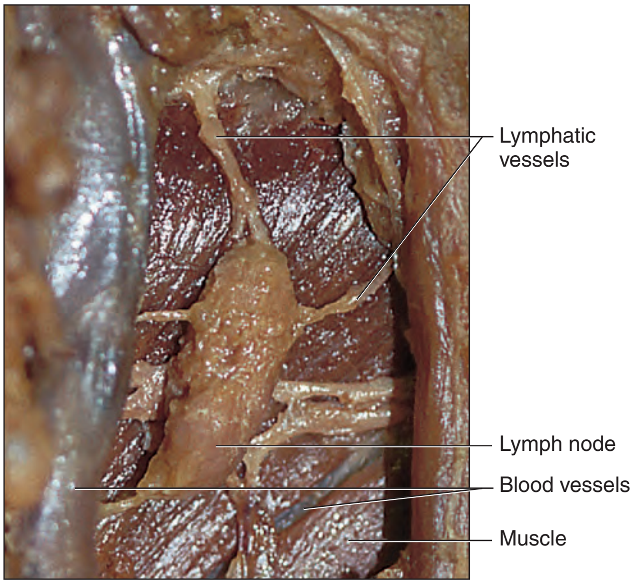


**FIGURE 14.7** Lymph enters and leaves a lymph node through lymphatic vessels.

A *capsule* of connective tissue encloses each lymph node and subdivides it into compartments. Lymph nodes contain large numbers of lymphocytes (B cells and T cells) and macrophages that fight invading microorganisms. Masses of B cells and macrophages in the cortex are contained within **lymphatic nodules**, also called lymphatic follicles, the functional units of the lymph node. The spaces within a node, called **lymphatic sinuses,** provide a complex network of chambers and channels through which lymph circulates.

Lymph nodes are generally in groups or chains along the paths of the larger lymphatic vessels throughout the body, but are absent in the central nervous system. Figure 14.8 shows the major locations of lymph nodes.

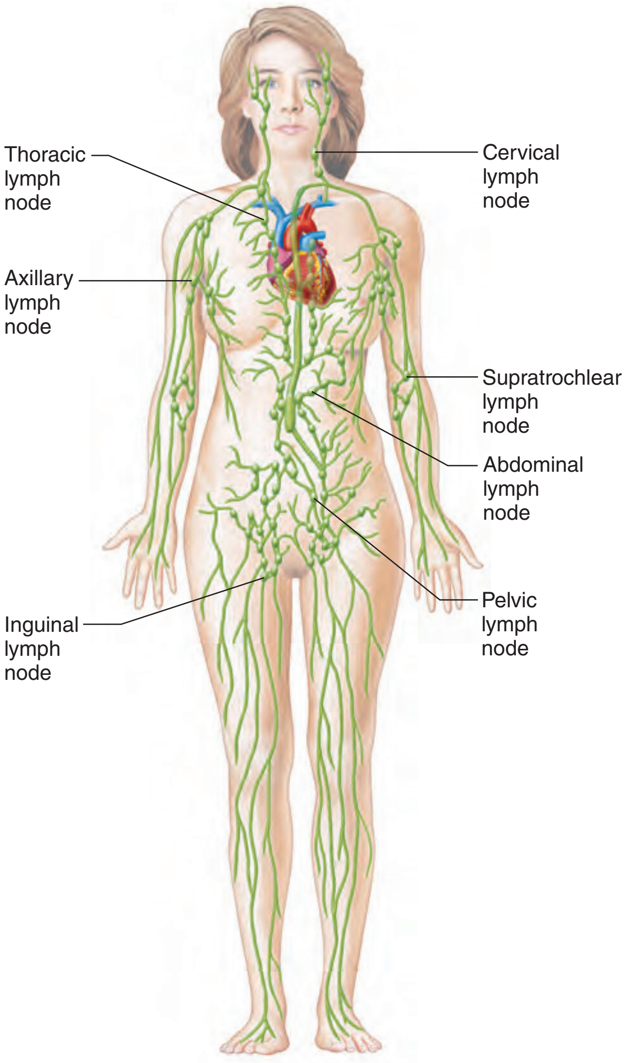


**FIGURE 14.8** Locations of major lymph nodes.

Lymph nodes have two primary functions: (1) filtering potentially harmful particles from lymph before returning it to the bloodstream, and (2) monitoring body fluids (immune surveillance) provided by lymphocytes and macrophages. Along with red bone marrow, the lymph nodes are centers for lymphocyte production. Lymphocytes attack viruses, bacteria, and other parasitic cells that lymphatic vessels bring to the lymph nodes. Macrophages in the lymph nodes engulf and destroy foreign substances, damaged cells, and cellular debris.

Superficial lymphatic vessels inflamed by bacterial infection appear as red streaks beneath the skin, a condition called *lymphangitis*. Inflammation of the lymph nodes, called *lymphadenitis,* often follows. In *lymphadenopathy,* affected lymph nodes enlarge and may be quite painful.

**PRACTICE**

8. What is the size and shape of a lymph node?
9. Where are lymph nodes located and what are their functions?

## Thymus

The **thymus** (thī′mus) is a soft, bilobed gland enclosed in a connective tissue capsule and located anterior to the aorta and posterior to the upper part of the sternum (fig. 14.9*a*). The thymus is usually proportionately larger during infancy and early childhood, but shrinks after puberty and may be quite small in an adult. In elderly persons, adipose and connective tissues replace lymphatic tissue in the thymus.

Connective tissues extend inward from the surface of the thymus, subdividing it into *lobules* (fig. 14.9*b*). The lobules house many lymphocytes. Most of these cells (thymocytes) are inactive; however, some mature into *T lymphocytes* (T cells), which leave the thymus and provide immunity. Epithelial cells in the thymus secrete hormones called *thymosins,* which stimulate maturation of T lymphocytes.

**FACTS OF LIFE** By age seventy years, the thymus is one-tenth the size it was at the age of ten.

## Spleen

The **spleen** (splēn), the largest lymphatic organ, is in the upper left portion of the abdominal cavity, just inferior to the diaphragm and posterior and lateral to the stomach (fig. 14.9*a*). The spleen resembles a large lymph node and is subdivided into lobules. However, unlike the lymphatic sinuses of a lymph node, the spaces (venous sinuses) in the spleen are filled with blood instead of lymph.

The tissues within splenic lobules are of two types (fig. 14.10). The *white pulp* is distributed throughout the spleen in tiny islands. This tissue is composed of splenic nodules, which are similar to the lymphatic nodules in lymph nodes and are packed with lymphocytes. The *red pulp,* which fills the remaining spaces of the lobules, surrounds the venous sinuses. This pulp contains numerous red blood cells, which impart its color, plus many lymphocytes and macrophages.

Blood capillaries in the red pulp are quite permeable. Red blood cells can squeeze through the pores in these capillary walls and enter the venous sinuses. The older, more fragile red blood cells may rupture during this passage, and the resulting cellular debris is removed by phagocytic macrophages in the splenic

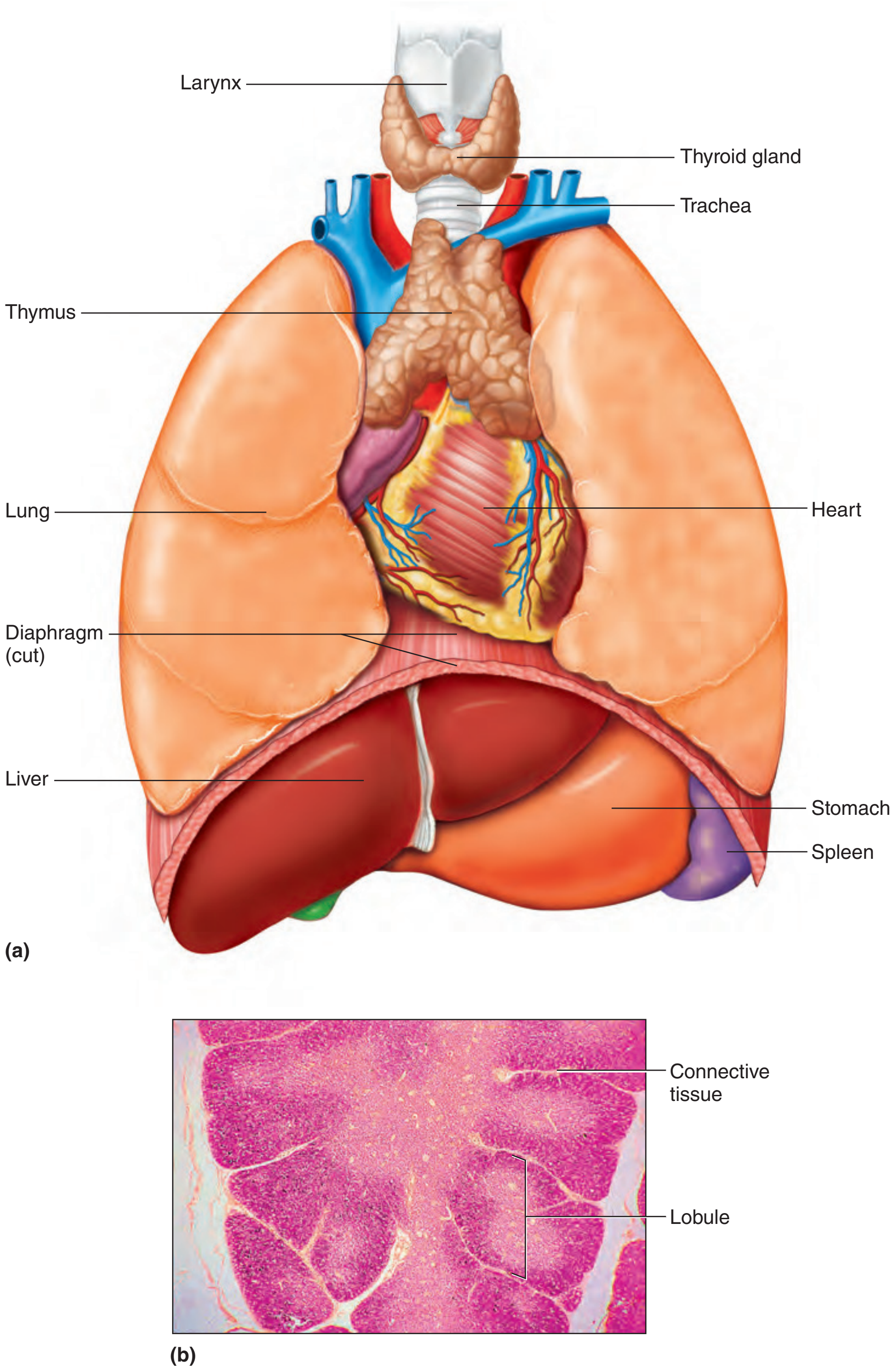

Larynx
Thyroid gland
Trachea
Thymus
Lung
Heart
Diaphragm (cut)
Liver
Stomach
Spleen
(a)
Connective tissue
Lobule
(b)

**FIGURE 14.9** APR Thymus and spleen. **(a)** The thymus is bilobed, located between the lungs and superior to the heart. The spleen is located inferior to the diaphragm and posterior and lateral to the stomach. **(b)** A section through the thymus (15×). Note how the thymus is subdivided into lobules.

sinuses. These macrophages also engulf and destroy foreign particles, such as bacteria, that may be carried in the blood as it flows through the splenic sinuses. Thus, the spleen filters blood much as the lymph nodes filter lymph.

## PRACTICE

10. Why are the thymus and the spleen considered organs of the lymphatic system?
11. What are the major functions of the thymus and the spleen?

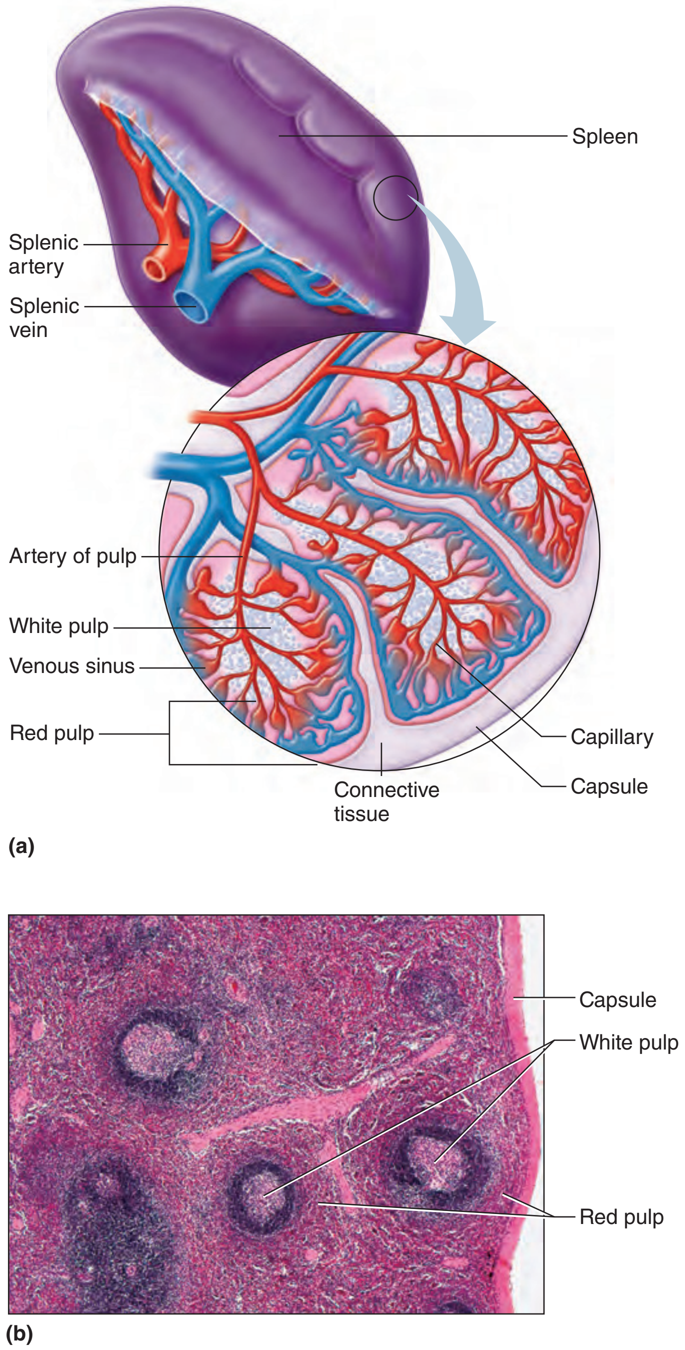


**FIGURE 14.10** APR Spleen. **(a)** The spleen resembles a large lymph node. **(b)** Light micrograph of the spleen (40×).

## 14.6 | Body Defenses Against Infection

The presence and multiplication of a disease-causing agent, or **pathogen** (path′o-jen), may cause an **infection.** Pathogens include viruses, bacteria, fungi, and protozoans.

> A virus is just a nucleic acid (DNA or RNA) inside a coat of proteins, and perhaps glycoproteins. An example of a DNA virus is herpes virus. RNA viruses cause influenza, polio, and measles. Viruses are simpler than cells, and reproduce using the organelles of the cells they infect to synthesize their own proteins. Bacteria are single, simple cells and cause many common infections, such as "Staph" and "Strep". Fungi may be single-celled or multi-celled. Yeast infections, ringworm, and athlete's foot are fungal infections. Protozoans are single, complex cells that cause diseases including malaria.

The human body can prevent the entry of pathogens or destroy them if they enter. Some mechanisms are quite general and protect against many types of pathogens, providing **innate (nonspecific) defense.** These mechanisms include species resistance, mechanical barriers, chemical barriers (enzyme action, interferon, and complement), natural killer cells, inflammation, phagocytosis, and fever. Other defense mechanisms are very precise, targeting specific pathogens and providing **adaptive (specific) defense,** or **immunity** (ĭ-mu′nĭ-te). Specialized lymphocytes that recognize foreign molecules (nonself antigens) in the body act against them. Innate and adaptive defense mechanisms work together to protect the body against infection. The innate defenses respond quite rapidly, while adaptive defenses develop more slowly.

## 14.7 | Innate (Nonspecific) Defenses

### Species Resistance

**Species resistance** refers to the fact that a given type of organism, or *species* (such as the human species, *Homo sapiens*), may be resistant to infectious diseases that affect other species because its cells do not have receptors for the pathogen or its tissues do not provide the temperature or chemical environment that a particular pathogen requires. For example, humans are infected by the infectious agents that cause measles, mumps, gonorrhea, and syphilis, but other animal species are not.

### Mechanical Barriers

The skin and mucous membranes lining the passageways of the respiratory, digestive, urinary, and reproductive systems create **mechanical barriers** that prevent the entrance of some infectious agents. As long as the skin and mucous membranes remain intact, many pathogens are unable to penetrate them. Hair traps infectious agents associated with the skin and mucous membranes, and sweat and mucus rinse away microorganisms. These mechanical barriers provide a *first line of defense*. The other innate defenses discussed in this section are part of the *second line of defense*.

## Chemical Barriers

Enzymes in body fluids provide a **chemical barrier** to pathogens. Gastric juice, for example, contains the protein-splitting enzyme pepsin and has a low pH due to the presence of hydrochloric acid (HCl) (see chapter 15, p. 421). The combined effect of pepsin and HCl kills many pathogens that enter the stomach. Similarly, tears contain the enzyme lysozyme, which destroys certain bacteria on the eyes. The accumulation of salt from perspiration also kills certain bacteria on the skin.

Lymphocytes and fibroblasts produce hormonelike peptides called **interferons** in response to viruses or tumor cells. Once released from the virus-infected cell, interferon binds to receptors on uninfected cells, stimulating them to synthesize proteins that block replication of a variety of viruses. Thus, interferon's effect is nonspecific. Interferons also stimulate phagocytosis and enhance the activity of other cells that help resist infections and the growth of tumors.

**Complement** (kom′ple-ment) is a group of proteins, in plasma and other body fluids, that interact in an expanding series of reactions or cascade. Activation of complement stimulates inflammation, attracts phagocytes, and enhances phagocytosis.

## Natural Killer (NK) Cells

**Natural killer** (NK) **cells** are a small population of lymphocytes different from the lymphocytes (T and B cells) that provide adaptive (specific) defense mechanisms (discussed later in this chapter). NK cells defend the body against various viruses and cancer cells by secreting cytolytic ("cell-cutting") substances called **perforins** that lyse the cell membrane, destroying the infected cell. NK cells also secrete chemicals that enhance inflammation.

## Inflammation

**Inflammation** (in″flah-ma′shun) is a tissue response to injury or infection, producing localized redness, swelling, heat, and pain. The redness is a result of blood vessel dilation that increases blood flow and volume in the affected tissues. This effect, coupled with an increase in the permeability of nearby capillaries and subsequent leakage of protein-rich fluid into tissue spaces, swells tissues (edema). The heat comes as blood enters from deeper body parts, which are warmer than the surface. Pain results from stimulation of nearby pain receptors.

Infected cells release chemicals that attract white blood cells to inflammation sites, where they phagocytize pathogens. Local heat speeds up phagocytic activity. In bacterial infections, the resulting mass of white blood cells, bacterial cells, and damaged tissue may form a thick fluid called **pus.**

Fluids called exudates also collect in inflamed tissues. These fluids contain fibrinogen and other blood-clotting factors. Clotting forms a network of fibrin threads in the affected region. Later, fibroblasts may arrive and secrete matrix components until the area is enclosed in a connective tissue sac. This walling off of the infected area helps inhibit the spread of pathogens and toxins to adjacent tissues.

## Phagocytosis

Phagocytosis removes foreign particles from the lymph as it moves from the interstitial spaces to the bloodstream. Phagocytes in the blood vessels and in the tissues of the spleen, liver, or bone marrow remove particles that reach the blood. Recall from chapter 12 (p. 334) that blood's most active phagocytic cells are *neutrophils* and *monocytes*. Chemicals released from injured tissues attract these cells (chemotaxis). Neutrophils engulf and digest smaller particles; monocytes phagocytize larger ones.

Monocytes that leave the bloodstream by diapedesis become *macrophages* (histiocytes), which may be *free* or *fixed* in various tissues. The fixed macrophages, which can divide and produce new macrophages, are found in the lymph nodes, spleen, liver, and lungs. Neutrophils, monocytes, and macrophages constitute the **mononuclear phagocytic system** (reticuloendothelial system).

## Fever

Fever is body temperature elevated above an individual's normal temperature due to an elevated setpoint. It is part of the innate defense because it makes the body inhospitable to certain pathogens. Higher body temperature causes the liver and spleen to sequester iron, which reduces the level of iron in the blood. Because bacteria and fungi require iron for normal metabolism, their growth and reproduction in a fever-ridden body slows and may cease. Also, phagocytic cells attack more vigorously when the temperature rises. For these reasons, low-grade fever of short duration may be a desired natural response, not a symptom to be treated aggressively with medications.

**PRACTICE**

12. What may cause an infection?
13. Explain seven innate (nonspecific) defense mechanisms.

## 14.8 Adaptive (Specific) Defenses, or Immunity

The *third line of defense,* **immunity** (ĭ-mu′nĭ-te), is resistance to specific pathogens or to their toxins or metabolic by-products. Lymphocytes and macrophages that recognize and remember specific foreign molecules carry out adaptive immune responses, which include the *cellular immune response* and the *humoral immune response.* Figure 14.11 shows a schematic representation of body defenses against pathogens.

### Antigens

**Antigens** (an′tĭ-jenz) are proteins, polysaccharides, glycoproteins, or glycolipids, that can elicit an immune response. Before birth, cells inventory the proteins and other large molecules in the body, learning to identify these as "self." The lymphatic system responds to "nonself," or foreign, antigens, but not normally to self antigens. Receptors on lymphocyte surfaces enable these cells to recognize nonself antigens.

The antigens most effective in eliciting an immune response are large and complex, with few repeating parts. A smaller molecule that cannot by itself stimulate an immune response may combine with a larger molecule, which makes it detectable to the immune system. Such a small molecule is called a **hapten** (hap′ten). Stimulated lymphocytes react either to the hapten or to the larger molecule of the combination. Hapten molecules are in drugs such as penicillin, in household and industrial chemicals, in dust particles, and in animal dander.

### Lymphocyte Origins

Lymphocyte production begins during fetal development (before birth and continues throughout life), with red bone marrow releasing unspecialized precursors to lymphocytes into the circulation. About half of these cells reach the thymus, where they specialize into **T lymphocytes,** or **T cells.** Some of these T cells constitute 70–80% of the circulating lymphocytes in blood. Other T cells reside in lymphatic organs and are particularly abundant in the lymph nodes, thoracic duct, and white pulp of the spleen.

Other lymphocytes remain in the red bone marrow until they differentiate into **B lymphocytes,** or **B cells.** The blood distributes B cells, which constitute 20–30% of circulating lymphocytes (fig. 14.12). B cells settle in lymphatic organs along with T cells and are abundant in the lymph nodes, spleen, bone marrow, and intestinal lining. Figure 14.13 illustrates B cell and T cell production. Table 14.1 compares the characteristics of T cells and B cells.

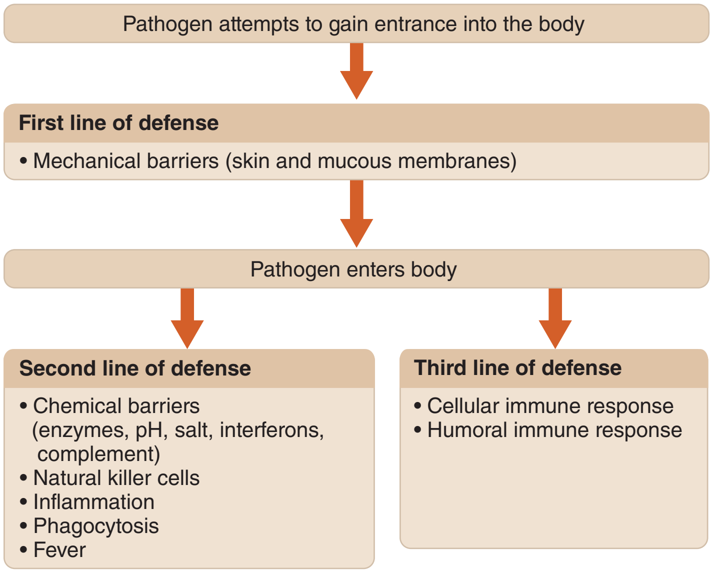

Pathogen attempts to gain entrance into the body
First line of defense
• Mechanical barriers (skin and mucous membranes)
Pathogen enters body
Second line of defense
• Chemical barriers (enzymes, pH, salt, interferons, complement)
• Natural killer cells
• Inflammation
• Phagocytosis
• Fever
Third line of defense
• Cellular immune response
• Humoral immune response

**FIGURE 14.11** Body defenses against pathogens.

**PRACTICE**

14. What is immunity?
15. What is the difference between an antigen and a hapten?
16. How do T cells and B cells originate?

### T Cells and the Cellular Immune Response

A lymphocyte must be activated before it can respond to an antigen. T cell activation requires that processed fragments of the antigen be attached to the surface of

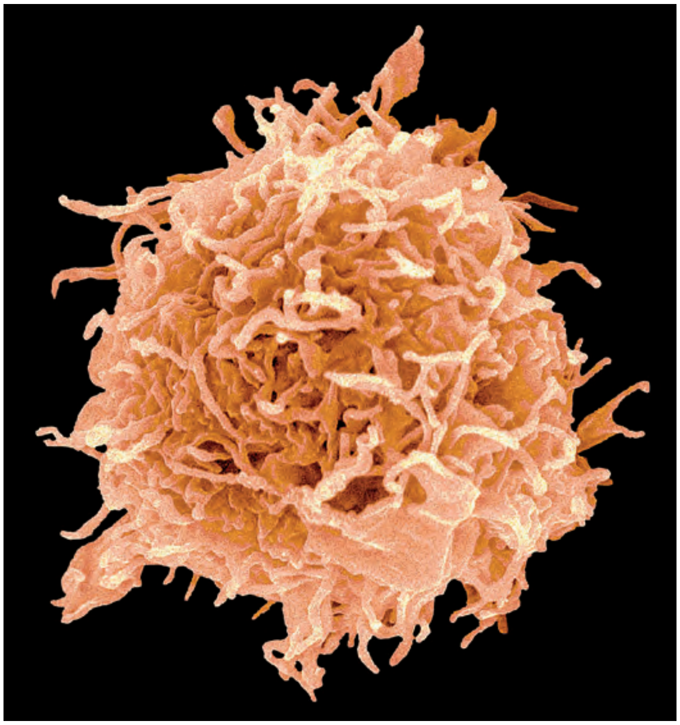


**FIGURE 14.12** Falsely colored scanning electron micrograph of a B cell (6,000×).

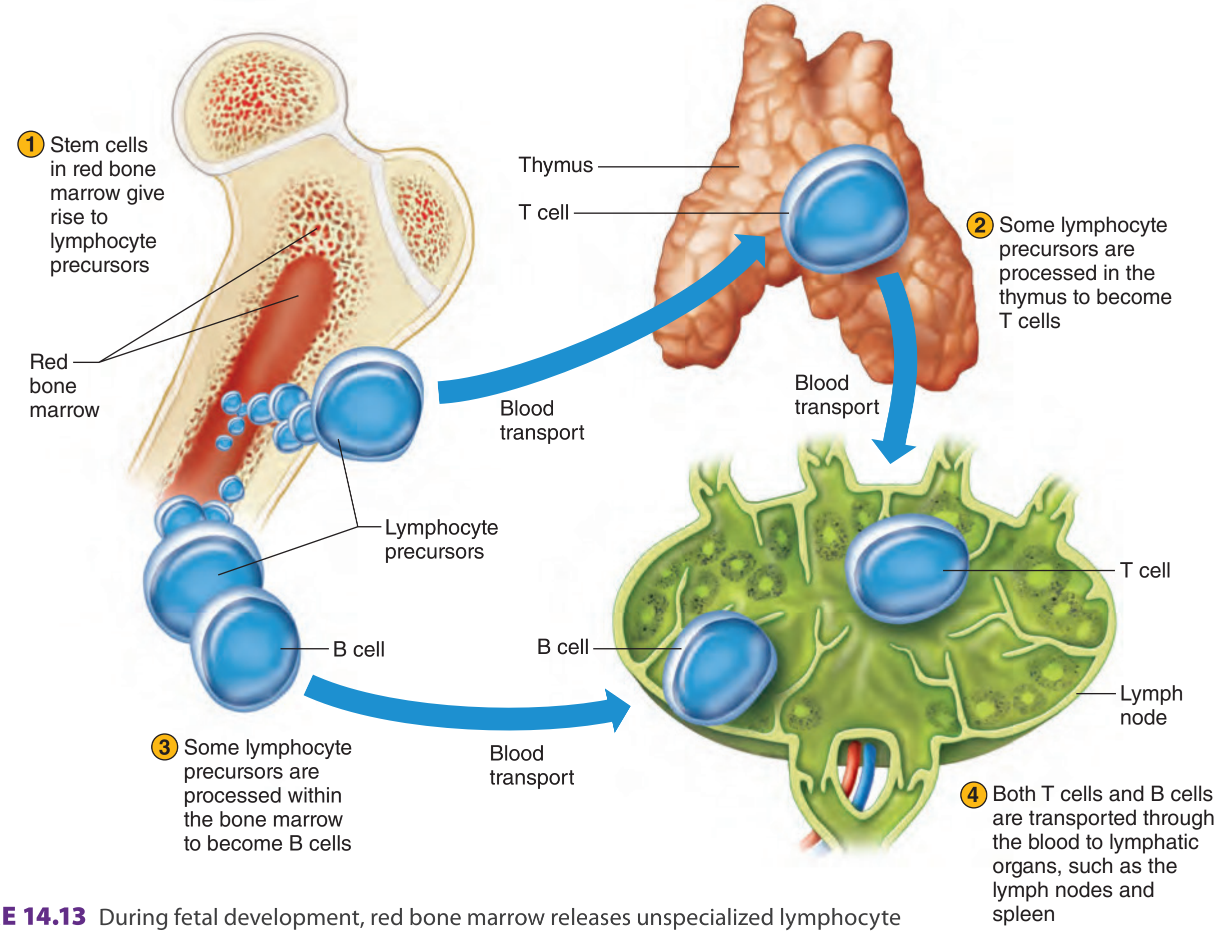

① Stem cells in red bone marrow give rise to lymphocyte precursors
Red bone marrow
Lymphocyte precursors
B cell
③ Some lymphocyte precursors are processed within the bone marrow to become B cells
Blood transport
Thymus
T cell
② Some lymphocyte precursors are processed in the thymus to become T cells
Blood transport
Blood transport
B cell
T cell
Lymph node
④ Both T cells and B cells are transported through the blood to lymphatic organs, such as the lymph nodes and spleen

**FIGURE 14.13** During fetal development, red bone marrow releases unspecialized lymphocyte precursors, which after processing specialize as T cells (T lymphocytes) or B cells (B lymphocytes). Lymphocyte production continues throughout life, with most T cells arising before puberty.

**TABLE 14.1** **A Comparison of T Cells and B Cells** APR

| Characteristic | T Cells | B Cells |
|---|---|---|
| Origin of undifferentiated cell | Red bone marrow | Red bone marrow |
| Site of differentiation | Thymus | Red bone marrow |
| Primary locations | Lymphatic tissues, 70–80% of the circulating lymphocytes in the blood | Lymphatic tissues, 20–30% of the circulating lymphocytes in the blood |
| Primary functions | Provides cellular immune response in which T cells interact directly with the antigens or antigen-bearing agents, to destroy them | Provides humoral immune response in which B cells interact indirectly, producing antibodies that destroy the antigens or antigen-bearing agents |

another type of cell, called an **antigen-presenting cell** (accessory cell). Macrophages, B cells, and several other cell types can be antigen-presenting cells.

T cell activation may occur when a macrophage phagocytizes a bacterium and digests it within a *phagolysosome* formed by the fusion of the vesicle containing the bacterium (phagosome) and a lysosome. Some of the resulting bacterial antigens are then displayed on the macrophage's membrane near certain protein molecules that are part of a group of proteins called the *major histocompatibility complex (MHC)*. MHC antigens help T cells recognize that a newly displayed antigen is foreign, not self.

Activated T cells interact directly with antigen-bearing cells. Such cell-to-cell contact is called the **cellular immune response,** or cell-mediated immunity. T cells (and some macrophages) also synthesize and secrete polypeptides called *cytokines* that enhance certain cellular responses to antigens. For example, *interleukin-1* and *interleukin-2* stimulate the synthesis of several other cytokines from other T cells. In addition, interleukin-1 helps activate T cells, whereas interleukin-2 causes T cells to proliferate. Certain other cytokines, called *colony-stimulating factors (CSFs),* stimulate leukocyte production in red bone marrow and activate macrophages. T cells may also secrete toxins that kill their antigen-bearing target cells, growth-inhibiting factors that prevent target cell growth, or interferon that inhibits the proliferation of viruses and tumor cells. Several types of T cells have distinct functions.

A specialized type of T cell, called a *helper T cell,* is activated when its antigen receptor combines with a displayed foreign antigen (fig. 14.14). Once activated, the helper T cell stimulates a B cell to produce antibodies that are specific for the displayed antigen.

Another type of T cell is a *cytotoxic T cell,* which recognizes and combines with nonself antigens that cancerous cells or virally infected cells display on their surfaces near certain MHC proteins. Cytokines from helper T cells activate the cytotoxic T cell. Next, the cytotoxic T cell proliferates, enlarging its **clone** (klōn) of cells, which is a group of genetically identical cells that descend from a single, original cell. Cytotoxic T cells then bind to the surfaces of antigen-bearing cells, where they release *perforin* protein that cuts porelike openings, destroying these cells. In this way, cytotoxic T cells continually monitor the body's cells, recognizing and eliminating tumor cells and cells infected with viruses. Cytotoxic T cells provide much of the immune system's defense against HIV infection, discussed in Clinical Application 14.1.

Certain cytotoxic T cells do not respond to a foreign antigen on first exposure, but remain as *memory cells* that provide for future immune protection. These memory cells immediately divide to yield more cytotoxic T cells and helper T cells upon subsequent exposure to the same antigen, often before symptoms arise.

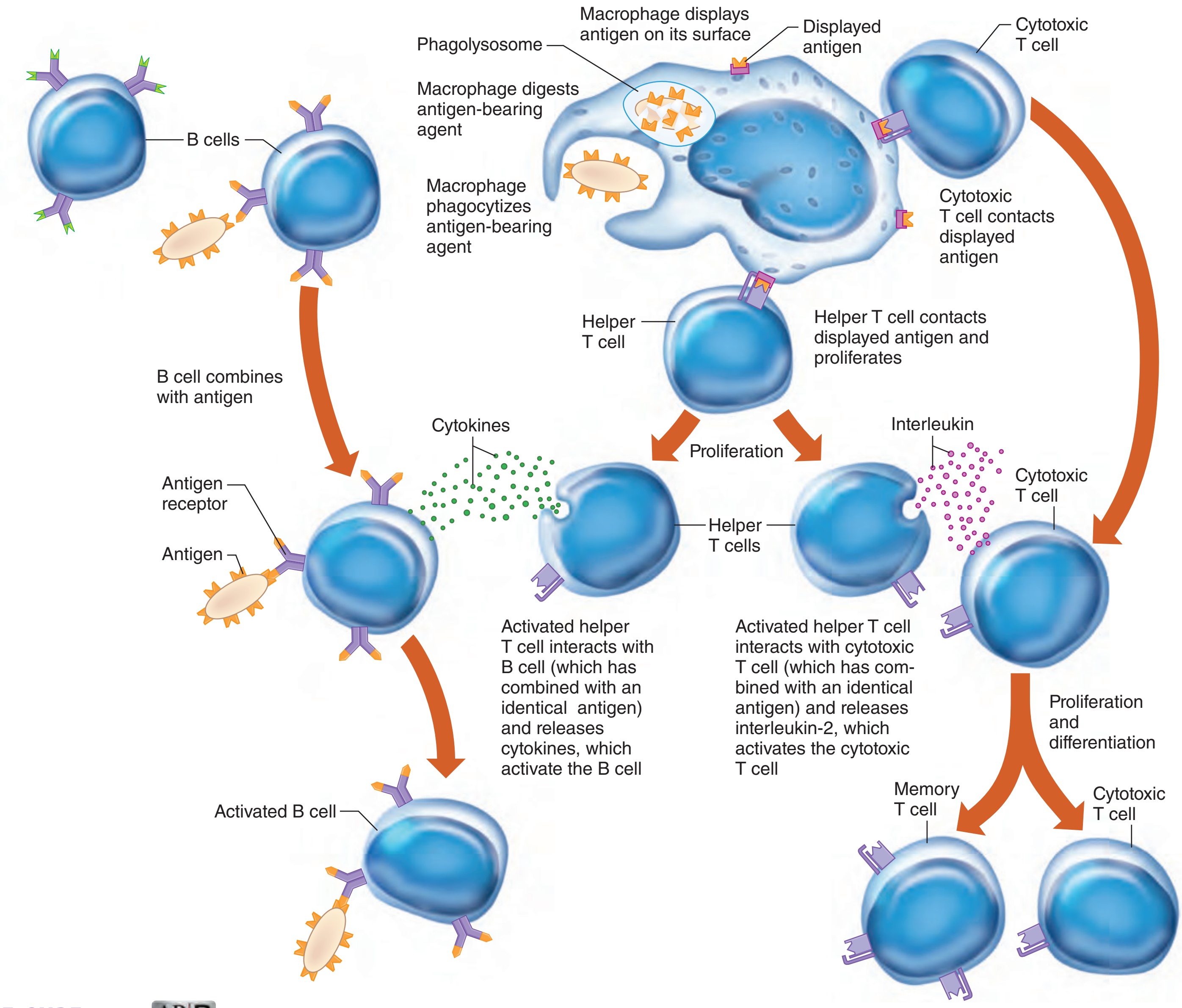

Macrophage displays antigen on its surface
Displayed antigen
Cytotoxic T cell
Phagolysosome
Macrophage digests antigen-bearing agent
B cells
Macrophage phagocytizes antigen-bearing agent
Cytotoxic T cell contacts displayed antigen
Helper T cell
Helper T cell contacts displayed antigen and proliferates
B cell combines with antigen
Cytokines
Proliferation
Interleukin
Cytotoxic T cell
Antigen receptor
Antigen
Helper T cells
Activated helper T cell interacts with B cell (which has combined with an identical antigen) and releases cytokines, which activate the B cell
Activated helper T cell interacts with cytotoxic T cell (which has combined with an identical antigen) and releases interleukin-2, which activates the cytotoxic T cell
Proliferation and differentiation
Activated B cell
Memory T cell
Cytotoxic T cell

**FIGURE 14.14** APR T and B cell activation.

CLINICAL APPLICATION **14.1**

## Immunity Breakdown: HIV/AIDS

In the early 1980s, physicians from large cities in the United States began reporting cases of rare infections in otherwise healthy young men. The conditions were opportunistic, taking advantage of a weakened immune system. These young men were the first to have been infected with the human immunodeficiency virus (HIV). Table 14A lists how HIV is, and isn't, spread. The HIV infection typically remains silent for several years and then may progress to *acquired immune deficiency syndrome (AIDS)* which starts with recurrent fever, weakness, and weight loss. Then, the opportunistic infections begin.

First HIV crosses a mucosal barrier, such as the lining of the anus or vagina. Then the virus enters macrophages. In these cells and later in helper T cells, the virus adheres with a surface protein, called gp120, to two receptors on the host cell surface, called CD4 and CCR5. Once the virus enters the cell, a viral enzyme, reverse transcriptase, builds a DNA strand complementary to the viral RNA sequence. Synthesis of a second DNA strand complementary to the first results in a viral DNA double helix, which is transported into the cell's nucleus and inserted into a chromosome. The cell uses the viral DNA sequences to mass produce pieces of HIV, which are then assembled into new viral particles that burst from the cell.

Once infected helper T cells start to rapidly die, bacterial infections begin because B cells aren't activated to produce antibodies. Much later in infection, HIV variants arise that bind receptors on cytotoxic T cells, killing them too. Loss of these cells renders the body vulnerable to other infections and to cancers.

HIV replicates quickly and alters its surface features in ways that evade recognition and attack by the immune system. The virus is especially prone to mutations because it cannot repair DNA replication errors. The immune system cannot keep up, with antibodies against one viral variant useless against another.

Within days of infection, HIV variants can arise that resist the drugs used to treat HIV infection and AIDS. Combining drugs that act at different steps in infection minimizes the number of viruses (viral load) and delays symptom onset and progression. These drugs block HIV from binding to cells, fusing with the cell membrane, entering the cell, replicating its genetic material, or processing viral proteins to functional sizes. Many people with HIV infection who use retroviral drugs can keep their viral levels low enough to stay healthy. Preliminary evidence suggests that aggressive treatment of newborns can lead to undetectable levels of HIV years later. More than 200 drugs are also available to treat AIDS-associated opportunistic infections and cancers.

Developing a vaccine against HIV has been challenging, both because of the great variability of HIV and the difficulty of testing the vaccine. A live vaccine is too dangerous; and a killed vaccine does not generate a sufficient immune response. HIV infection may be prevented other ways, including education about reducing risk factors, and giving pregnant women antiretroviral drugs to prevent transmission to offspring.

**TABLE 14A HIV Transmission**

| How HIV Is Transmitted |
|---|
| Sexual contact, particularly anal intercourse, but also vaginal intercourse and oral sex |
| Contaminated needles (intravenous drug use, injection of anabolic steroids, accidental needle stick in medical setting) |
| During birth from infected mother |
| Breast milk from infected mother |
| Receiving infected blood or other tissue (precautions usually prevent this) |
| **How HIV Is Not Transmitted** |
| Casual contact (social kissing, hugging, handshakes) |
| Objects (toilet seats, deodorant sticks, doorknobs) |
| Mosquitoes |
| Sneezing and coughing |
| Sharing food |
| Swimming in the same water |
| Donating blood |

**PRACTICE**

17. How do T cells become activated?
18. What are some functions of cytokines?
19. Name three types of T cells.
20. How do cytotoxic T cells destroy cells bearing foreign antigens?

## B Cells and the Humoral Immune Response

When a B cell encounters an antigen whose molecular shape fits the shape of the B cell's antigen receptors, it becomes activated. In response to the receptor-antigen combination, the B cell divides repeatedly, expanding its clone. However, most of the time B cell activation requires T cell "help."

When an activated helper T cell encounters a B cell already combined with a foreign antigen identical to the one that activated the helper T cell, the helper cell releases certain cytokines. These cytokines stimulate the B cell to proliferate, enlarging its clone of antibody-producing cells (fig. 14.15). The cytokines also attract macrophages and leukocytes into inflamed tissues and help keep them there.

Some members of the activated B cell's clone differentiate further into **plasma cells,** which produce and secrete large globular proteins called **antibodies** (an′tĭ-bod″ēz), or **immunoglobulins** (im″u-no-glob′u-linz), similar in structure to the antigen-receptor molecules on the original B cell's surface. Body fluids carry antibodies, which then react in various ways to destroy specific antigens or antigen-bearing particles. This antibody-mediated immune response is called the **humoral immune response** ("humoral" refers to fluid). Table 14.2 summarizes the steps leading to antibody production as a result of B cell and T cell activities.

**FACTS OF LIFE** A plasma cell secretes up to 2,000 identical antibody molecules per second.

Other members of the activated B cell's clone differentiate further into *memory cells*. Like memory T cells, these memory B cells respond rapidly to subsequent exposure to a specific antigen.

An individual's B cells can produce more than 1,000,000,000 different antibodies, each reacting against

**FIGURE 14.15** An activated B cell proliferates after stimulation by cytokines released from helper T cells. The B cell's clone enlarges. Some cells of the clone give rise to antibody-secreting plasma cells and others to dormant memory cells.

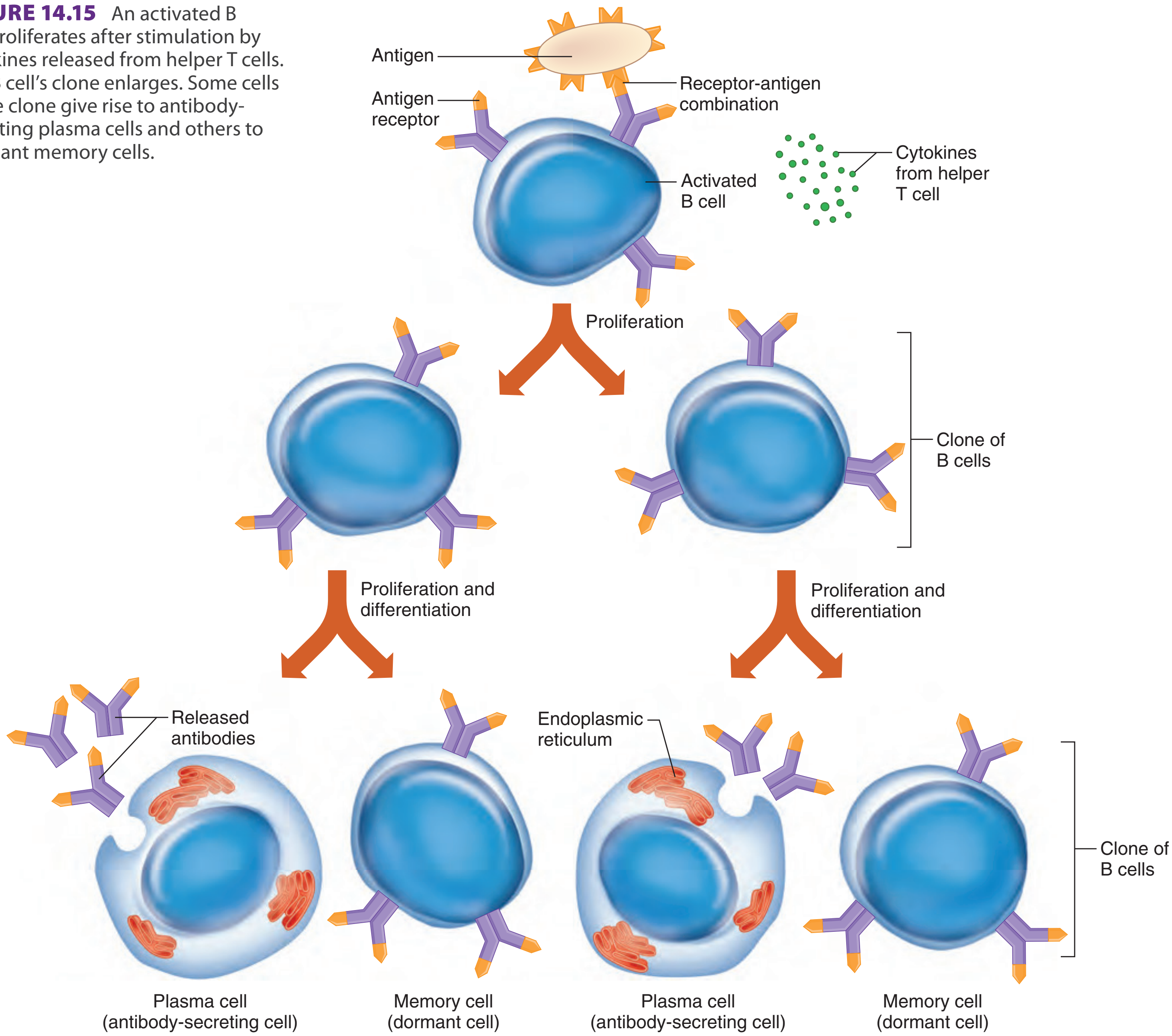

Antigen
Antigen receptor
Receptor-antigen combination
Activated B cell
Cytokines from helper T cell
Proliferation
Clone of B cells
Proliferation and differentiation
Proliferation and differentiation
Released antibodies
Endoplasmic reticulum
Clone of B cells
Plasma cell (antibody-secreting cell)
Memory cell (dormant cell)
Plasma cell (antibody-secreting cell)
Memory cell (dormant cell)

**TABLE 14.2 Steps in Antibody Production**

**B Cell Activities**

1. Antigen-bearing agents enter tissues.
2. B cell encounters an antigen that fits its antigen receptors.
3. Either alone or more often in conjunction with helper T cells, the B cell is activated. The B cell proliferates, enlarging its clone.
4. Some of the newly formed B cells differentiate further to become plasma cells.
5. Plasma cells synthesize and secrete antibodies whose molecular structure is similar to the activated B cell's antigen receptors.

**T Cell Activities**

1. Antigen-bearing agents enter tissues.
2. An accessory cell, such as a macrophage, phagocytizes the antigen-bearing agent, and the macrophage's lysosomes digest the agent.
3. Antigens from the digested antigen-bearing agents are displayed on the membrane of the accessory cell.
4. Helper T cell becomes activated when it encounters a displayed antigen that fits its antigen receptors.
5. Activated helper T cell releases cytokines when it encounters a B cell that has previously combined with an identical antigen-bearing agent.
6. Cytokines stimulate the B cell to proliferate.
7. Some of the newly formed B cells give rise to cells that differentiate into antibody-secreting plasma cells.

a specific antigen. The enormity and diversity of the antibody response defends against many pathogens.

## Types of Antibodies

Antibodies (immunoglobulins) are soluble, globular proteins that constitute the *gamma globulin* fraction of plasma proteins (see chapter 12, p. 338). Of the five major types of immunoglobulins, the most abundant are immunoglobulin G, immunoglobulin A, and immunoglobulin M.

*Immunoglobulin G (IgG)* is in plasma and tissue fluids and is particularly effective against bacteria, viruses, and toxins. It also activates *complement.*

*Immunoglobulin A (IgA)* is commonly found in exocrine gland secretions. It is in breast milk, tears, nasal fluid, gastric juice, intestinal juice, bile, and urine.

*Immunoglobulin M (IgM)* is a type of antibody present in plasma in response to contact with certain antigens in foods or bacteria. The antibodies anti-A and anti-B, described in chapter 12 (p. 343), are examples of IgM. IgM also activates complement.

*Immunoglobulin D (IgD)* is found on the surfaces of most B cells, especially those of infants. IgD is important in activating B cells.

*Immunoglobulin E (IgE)* is in exocrine secretions with IgA. It is associated with allergic reactions, which are described later in this section (see p. 403).

A newborn does not yet have its own antibodies, but does retain for a while IgG that passed through the placenta from the mother. These maternal antibodies protect the infant against some illnesses to which the mother is immune. As the maternal antibody supply falls, the infant begins to manufacture its own antibodies. The newborn also receives IgA from colostrum, a substance secreted from the mother's breasts for the first few days after birth, and then from breast milk. Antibodies in colostrum protect against certain digestive and respiratory infections.

**PRACTICE**

21. How are B cells activated?
22. How does the antibody response protect against diverse infections?
23. Which immunoglobulins are most abundant, and how do they differ from each other?

## Antibody Actions

In general, antibodies react to antigens in three ways. Antibodies directly attack antigens, activate complement, or stimulate localized changes (inflammation) that help prevent the spread of pathogens or cells bearing foreign antigens.

In a direct attack, antibodies combine with antigens, causing them to clump (agglutination) or to form insoluble substances (precipitation). Such actions make it easier for phagocytic cells to recognize and engulf the antigen-bearing agents and eliminate them. In other instances, antibodies cover the toxic portions of antigen molecules and neutralize their effects (neutralization). However, under normal conditions, direct antibody attack is not as important as complement activation in protecting against infection.

When certain IgG or IgM antibodies combine with antigens, they expose reactive sites on antibody molecules. This triggers a series of reactions, leading to activation of the complement proteins, which in turn produce a variety of effects. These include: coating the antigen-antibody complexes (opsonization), making the complexes more susceptible to phagocytosis; attracting macrophages and neutrophils into the region (chemotaxis); rupturing membranes of foreign cells (lysis); agglutination of antigen-bearing cells; and neutralization of viruses by altering their molecular structure, making them harmless (fig. 14.16). Other proteins promote inflammation, which helps prevent the spread of infectious agents.

## PRACTICE

24. In what general ways do antibodies function?
25. How is complement activated?
26. What are the effects of complement activation?

## Immune Responses

Activation of B cells or T cells after first encountering the antigens for which they are specialized to react constitutes a **primary immune response.** During such a response, plasma cells release antibodies (IgM, followed by IgG) into the lymph. The antibodies are transported to the blood and then throughout the body, where they help destroy antigen-bearing agents. Production and release of antibodies continues for several weeks.

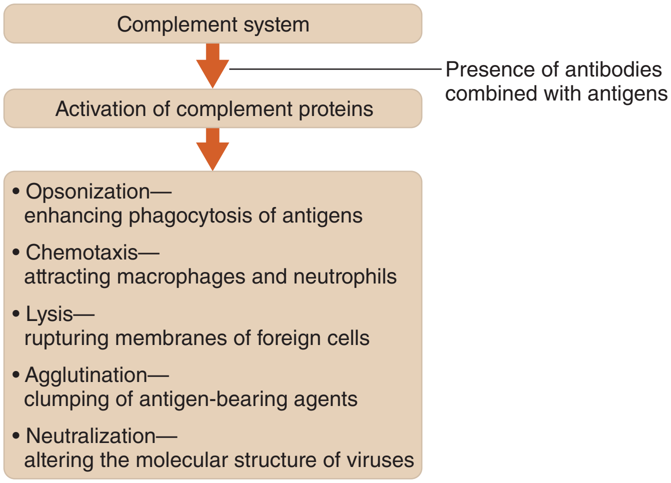

Complement system
Presence of antibodies combined with antigens
Activation of complement proteins
• Opsonization— enhancing phagocytosis of antigens
• Chemotaxis— attracting macrophages and neutrophils
• Lysis— rupturing membranes of foreign cells
• Agglutination— clumping of antigen-bearing agents
• Neutralization— altering the molecular structure of viruses

**FIGURE 14.16** Actions of the complement system.

Following a primary immune response, some of the B cells produced during proliferation of the clone remain dormant as memory cells (see fig. 14.15). If the same antigen is encountered again, the clones of these memory cells enlarge, and they can respond rapidly with IgG to the antigen to which they were previously sensitized. These memory B cells, along with the memory T cells, produce a **secondary immune response.**

As a result of a primary immune response, detectable concentrations of antibodies usually appear in the blood plasma five to ten days after exposure to antigens. If the same type of antigen is encountered later, a secondary immune response may produce the same antibodies within a day or two (fig. 14.17). Although newly formed antibodies may persist in the body for only a few months or years, memory cells live much longer.

## Practical Classification of Immunity

Adaptive, also known as acquired, immunity can arise in response to natural events or be induced artificially by injection. Both naturally and artificially acquired immunities can be either active or passive. Active immunity results when the person produces an immune response (including memory cells) to the antigen; it is long-lasting. Passive immunity occurs when a person receives antibodies produced by another individual. Because the person does not produce an immune response, passive immunity is short-term, and the individual will be susceptible upon exposure to the antigen at some later date.

*Naturally acquired active immunity* occurs when a person exposed to a pathogen develops a disease. Resistance to that pathogen is the result of a primary immune response.

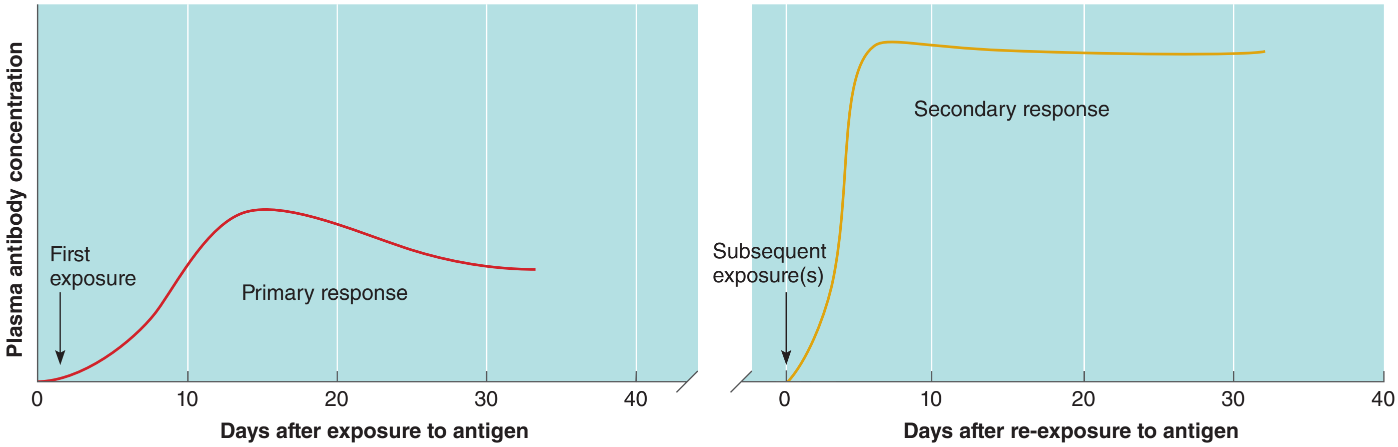


**FIGURE 14.17** A primary immune response occurs after the first exposure to an antigen. A secondary immune response occurs after subsequent exposure(s) to the same antigen. The break in the timeline represents a time lapse between exposure(s) to the antigen.

Q *Which immune response produces antibodies to a specific antigen more rapidly, primary or secondary?*
**Answer can be found in Appendix F on page 582.**

A **vaccine** (vak′sēn) is a preparation that produces another type of active immunity. A vaccine might consist of bacteria or viruses that have been killed or weakened so that they cannot cause a serious infection, or only molecules unique to the pathogens. A vaccine might also be a toxoid, which is a toxin from an infectious organism that has been chemically altered to destroy its dangerous effects. Whatever its composition, a vaccine includes the antigens that stimulate a primary immune response, but does not produce symptoms of disease and the associated infections. A vaccine causes a person to develop *artificially acquired active immunity.*

Specific vaccines stimulate active immunity against a variety of diseases, including typhoid fever, cholera, whooping cough, diphtheria, tetanus, polio, chickenpox, measles (rubeola), German measles (rubella), mumps, influenza, hepatitis A, hepatitis B, and bacterial pneumonia. Vaccines have virtually eliminated naturally acquired smallpox from the world.

A person who has been exposed to infection may require protection against a disease-causing microorganism before active immunity has had the time to develop. An injection of antiserum (antibody-rich serum) may help. More concentrated antibodies may be obtained by separating gamma globulins from the plasma of persons who have already developed immunity against the particular disease. Injection of either antiserum or gamma globulins provides *artificially acquired passive immunity.*

During pregnancy, certain antibodies (IgG) pass from the maternal blood into the fetal bloodstream. As a result, the fetus acquires limited immunity against pathogens that the pregnant woman has developed active immunities against. The fetus thus has *naturally acquired passive immunity,* which may last for six months to a year after birth. Table 14.3 summarizes the types of acquired immunity.

## PRACTICE

27. Distinguish between a primary and a secondary immune response.
28. Distinguish between active and passive immunity.

## Allergic Reactions APR

An allergic reaction is an immune response to a nonharmful substance. Allergic reactions are similar to immune responses because they sensitize lymphocytes and provide antibodies that may combine with antigens. However, unlike normal immune responses, allergic reactions can damage tissues. Antigens that trigger allergic responses are called **allergens** (al′er-jenz). Allergies can be classified by how quickly they follow exposure to the allergen.

An *immediate-reaction allergy* occurs within minutes after contact with an allergen, and affects people who have an inherited tendency to overproduce IgE antibodies in response to certain antigens. IgE normally constitutes only a tiny fraction of plasma proteins. An immediate-reaction allergy activates B cells, which become sensitized when the allergen is first encountered. Subsequent exposures to the allergen trigger allergic reactions. In the initial exposure, IgE attaches to the cell membranes of widely distributed mast cells and basophils. When a subsequent allergen-antibody reaction occurs, these cells release allergy mediators such as *histamine, prostaglandin* $D_2$, and *leukotrienes.* These substances cause a variety of physiological effects, including dilation of blood vessels, increased vascular permeability that swells tissues, contraction of bronchial and intestinal smooth muscle, and increased mucus production. The overall result is an inflammation reaction that is responsible for the symptoms of the allergy, such as hives, hay fever, asthma, eczema, or gastric disturbances. Anaphylactic shock is a severe form of immediate-reaction allergy in which mast cells release allergy mediators throughout the body. The entire body itches and breaks

**TABLE 14.3 Practical Classification of Immunity**

| Type | Mechanism | Result |
|---|---|---|
| Naturally acquired active immunity | Exposure to live pathogens | Stimulation of an immune response with symptoms of a disease |
| Artificially acquired active immunity | Exposure to a vaccine containing weakened or dead pathogens or their components | Stimulation of an immune response without the severe symptoms of a disease |
| Naturally acquired passive immunity | Antibodies passed to fetus from pregnant woman with active immunity or to newborn through colostrum or breast milk from a woman with active immunity | Short-term immunity for newborn without stimulating an immune response |
| Artificially acquired passive immunity | Injection of antiserum or gamma globulins | Short-term immunity without stimulating an immune response |

out in red hives. Vomiting and diarrhea may follow. The face, tongue, and larynx begin to swell, and breathing becomes difficult as happened to the woman with a peanut allergy in the chapter opening vignette. Unless the person receives an injection of epinephrine (adrenalin) and in some cases a tracheotomy (an incision into the windpipe to restore breathing) consciousness may fade and death will follow within minutes. Common triggers of anaphylactic shock are insect stings and allergy to penicillin.

A *delayed-reaction allergy* results from repeated exposure of the skin to certain chemicals—commonly, household or industrial chemicals or ingredients of some cosmetics. After repeated contact, the presence of the foreign substance activates T cells, many of which collect in the skin. The T cells and the macrophages they attract release chemical factors, which in turn cause eruptions and inflammation of the skin (dermatitis). This reaction is called *delayed* because it usually takes about 48 hours to occur. A delayed-reaction allergy may affect anyone. An example is seen in how some people react to poison ivy.

Common allergic conditions, such as asthma, eczema, and hay fever, have become more prevalent in recent years. Studies have shown that children raised on farms, with early exposure to many microbes to which the immune system reacts, are significantly less likely to develop allergies than children not raised on farms. This observation is part of the "hygiene hypothesis," that too much cleanliness may prevent the immune system from fully developing during childhood.

## Transplantation and Tissue Rejection

Transplantation of tissues or an organ, such as the skin, kidney, heart, or liver, from one person to another can replace a nonfunctional, damaged, or lost body part. However, the recipient's immune system may recognize the donor's cell surfaces as foreign and attempt to destroy the transplanted tissue, causing a **tissue rejection reaction.**

Tissue rejection resembles the cellular immune response against a foreign antigen. The greater the antigenic difference between the cell surface molecules (MHC antigens, discussed on page 397) of the recipient tissues and the donor tissues, the more rapid and severe the rejection reaction. Matching donor and recipient tissues can minimize the rejection reaction.

*Immunosuppressive drugs* are used to reduce rejection of transplanted tissues. These drugs interfere with the recipient's immune response by suppressing formation of antibodies or production of T cells, thereby dampening the humoral and cellular immune responses which may also cause the recipient to be more susceptible to infection. Immunosuppressive drugs were once given for the rest of the organ recipient's life. However, experience has shown that it is often better to begin immunosuppressive therapy before the transplant, and possibly end it after a few years, especially if the recipient has also received bone marrow stem cells from the donor. Lifelong immunosuppressants may disturb the process of the tissues from recipient and donor accepting each other.

**FACTS OF LIFE** Donated organs must be transplanted quickly. How long can donated organs be maintained outside the body under ideal conditions?

- A heart lasts three to five hours.
- A liver lasts ten hours.
- A kidney lasts twenty-four to forty-eight hours.

## Autoimmunity

The immune system can turn against itself, and become unable to distinguish a particular self antigen from a nonself antigen, producing **autoantibodies** and cytotoxic T cells that attack and damage the body's tissues and organs. This reaction against self is called **autoimmunity.** The specific nature of an autoimmune disorder reflects the cell types that are the target of the immune attack. In type 1 (insulin dependent) diabetes mellitus the target is beta cells in the pancreas, in rheumatoid arthritis the target is tissues within the joints, and in systemic lupus erythematosus the target is DNA and proteins associated with it. About 5% of the population have an autoimmune disorder.

Why might the immune system attack body tissues? Perhaps a virus, while replicating inside a human cell, takes proteins from the host cell's surface and incorporates them onto its own surface. When the immune system "learns" the surface of the virus in order to destroy it, it also learns to attack the human cells that normally bear those particular proteins. Another explanation of autoimmunity is that somehow T cells never learn to distinguish self from nonself. A third possible route of autoimmunity is when a nonself antigen coincidentally resembles a self antigen. This is what happens when an infection by *Streptococcus* bacteria triggers inflammation of heart valves, as mentioned in chapter 13 (p. 353). Clinical Application 14.2 discusses how some disorders thought to be autoimmune may be the result of lingering fetal cells.

### PRACTICE

29. How are allergic reactions and immune reactions similar yet different?
30. How does a tissue rejection reaction involve an immune response?
31. How is autoimmunity an abnormal functioning of the immune response?

## CLINICAL APPLICATION 14.2

### Persisting Fetal Cells and Autoimmunity

Some disorders thought to be autoimmune may have a stranger cause—fetal cells persisting in a woman's circulation, for decades. In response to an as yet unknown trigger, the fetal cells, perhaps "hiding" in a tissue such as skin, emerge, stimulating antibody production. The resulting antibodies and symptoms appear to be an autoimmune disorder. This situation of persisting fetal cells provoking an immune response is seen in a disorder called scleroderma, which means "hard skin."

Scleroderma, which is four times more common in women, typically begins between ages forty-five and fifty-five. It is described as "the body turning to stone." Symptoms include fatigue, swollen joints, stiff fingers, and a masklike face. The hardening may affect blood vessels, the lungs, and the esophagus. Clues that scleroderma is a delayed response to persisting fetal cells include the following observations:

- It is much more common among women past their reproductive years.
- Mothers who have scleroderma and their sons have cell surfaces that are more similar than those of unaffected mothers and their sons. Perhaps the similarity of cell surfaces enables the fetal cells to escape destruction by the woman's immune system, yet they are different enough to trigger an immune response. (Female fetal cells probably have the same effect, but they are not observable because the method used to detect fetal cells identifies a DNA sequence unique to the Y chromosome, which is only in males.)
- Symptoms resemble those of graft-versus-host disease (GVHD), in which transplanted tissue produces chemicals that destroy the recipient's tissues.

## Summary Outline

### 14.1 Introduction (p. 387)

*The lymphatic system is closely associated with the cardiovascular system. It transports excess tissue fluid to the bloodstream, absorbs fats, and helps defend the body against disease-causing agents.*

### 14.2 Lymphatic Pathways (p. 388)

1. Lymphatic capillaries
    a. Lymphatic capillaries are microscopic, closed-ended tubes that extend into interstitial spaces.
    b. They receive tissue fluid through their thin walls.
2. Lymphatic vessels
    a. Lymphatic vessels are formed by the merging of lymphatic capillaries.
    b. Lymphatic vessels have walls similar to those of veins, only thinner, and possess valves that prevent backflow of lymph.
    c. Larger lymphatic vessels lead to lymph nodes and then merge into lymphatic trunks.
3. Lymphatic trunks and collecting ducts
    a. Lymphatic trunks lead to two collecting ducts—the thoracic duct and the right lymphatic duct.
    b. Collecting ducts empty into the subclavian veins.

### 14.3 Tissue Fluid and Lymph (p. 389)

1. Tissue fluid formation
    a. Tissue fluid originates from plasma and includes water and dissolved substances that have passed through the blood capillary wall.
    b. It generally lacks large proteins, but some smaller proteins are filtered out of blood capillaries into interstitial spaces.
    c. As the protein concentration of tissue fluid increases, colloid osmotic pressure increases.
2. Lymph formation and function
    a. Increasing hydrostatic pressure within interstitial spaces forces some tissue fluid into lymphatic capillaries, and this fluid becomes lymph.
    b. Lymph returns small protein molecules to the bloodstream and transports foreign particles to lymph nodes.

### 14.4 Lymph Movement (p. 390)

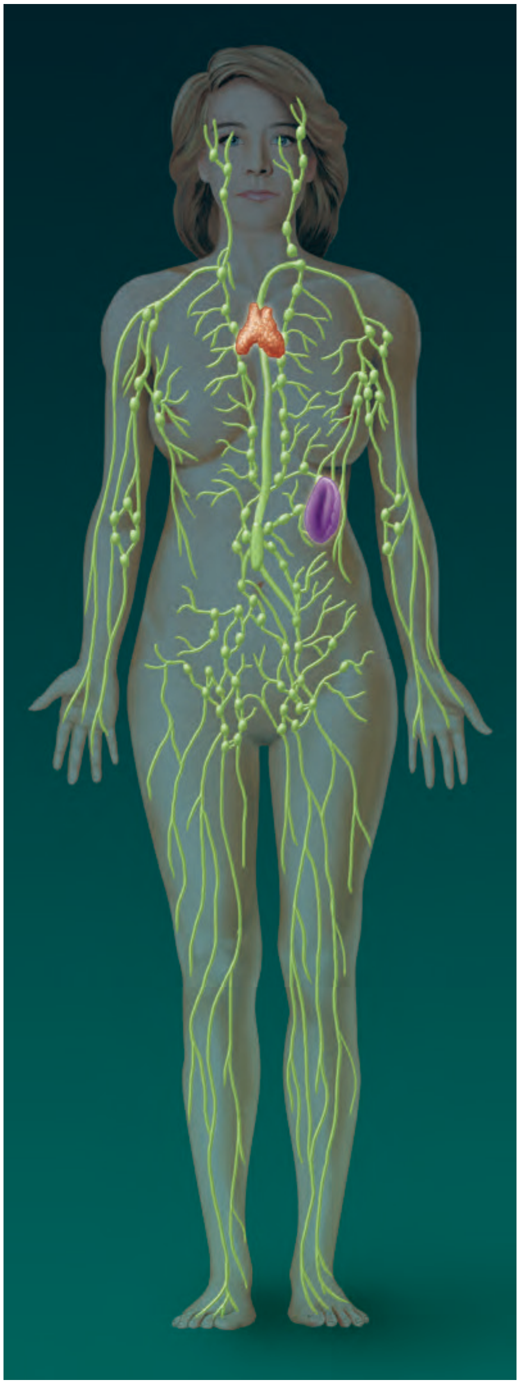
1. Lymph is under low pressure and may not flow readily without external aid.
2. Lymph is moved by the contraction of skeletal muscles, contraction of smooth muscle in the walls of large lymphatic trunks, and low pressure in the thorax created by breathing movements.

### 14.5 Lymphatic Tissues and Lymphatic Organs (p. 391)

*Unencapsulated lymphatic tissue includes the diffuse MALT (mucosa-associated lymphoid tissue), the tonsils, and appendix. The lymph nodes, thymus, and spleen are encapsulated lymphatic organs.*

1. Lymph nodes
    a. Lymph nodes are subdivided into nodules.
    b. Nodules contain masses of lymphocytes and macrophages.
    c. Lymph nodes aggregate in groups or chains along the paths of larger lymphatic vessels.
    d. Lymph nodes filter potentially harmful foreign particles from lymph.
    e. Lymph nodes are centers for the production of lymphocytes, and they also contain phagocytic cells.
2. Thymus
    a. The thymus, located anterior to the aorta and posterior to the upper part of the sternum, is composed of lymphatic tissue subdivided into lobules.
    b. It slowly shrinks after puberty.
    c. Some lymphocytes leave the thymus and provide immunity.
3. Spleen
    a. The spleen, just inferior to the diaphragm and posterior and lateral to the stomach, resembles a large lymph node subdivided into lobules.
    b. Spaces within splenic lobules are filled with blood.
    c. The spleen contains many macrophages, which filter foreign particles and damaged red blood cells from blood.

# Lymphatic System

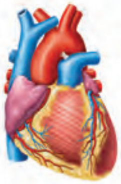


The lymphatic system is an important link between tissue fluid and the plasma; it also plays a major role in the body's response to infection.

## Integumentary System

The skin is a first line of defense against infection.

## Cardiovascular System



The lymphatic system returns tissue fluid to the bloodstream. Lymph originates as tissue fluid, formed by the action of blood pressure.

## Skeletal System

Cells of the immune system originate in the bone marrow.

## Digestive System

Lymph plays a major role in the absorption of fats.

## Muscular System

Muscle action helps pump lymph through the lymphatic vessels.

## Respiratory System

Cells of the immune system patrol the respiratory system to defend against infection.

## Nervous System

Stress may impair the immune response.

## Urinary System

The kidneys control the volume of extracellular fluid, including lymph.

## Endocrine System

Hormones stimulate lymphocyte production.

## Reproductive System

Special mechanisms inhibit the female immune system in its attack of sperm as foreign invaders.

### 14.6 Body Defenses Against Infection (p. 394)

*The body has innate (nonspecific) and adaptive (specific) defenses against infection.*

### 14.7 Innate (Nonspecific) Defenses (p. 394)

1. Species resistance
   Each species is resistant to certain diseases that may affect other species.
2. Mechanical barriers
   a. Mechanical barriers include the skin and mucous membranes, which block the entrance of some pathogens.
   b. Hair traps infectious agents; fluids such as tears, sweat, saliva, mucus, and urine wash away microorganisms before they can firmly attach.
3. Chemical barriers
   a. Enzymes in gastric juice and tears kill some pathogens.
   b. Interferons stimulate uninfected cells to synthesize antiviral proteins that stimulate phagocytosis, block proliferation of viruses, and enhance activity of cells that help resist infections and stifle tumor growth.
   c. Activation of complement proteins in plasma stimulates inflammation, attracts phagocytes, and enhances phagocytosis.
4. Natural killer cells
   Natural killer cells secrete perforins, which destroy cancer cells and cells infected with viruses.
5. Inflammation
   a. Inflammation is a tissue response to injury or infection, and includes localized redness, swelling, heat, and pain.
   b. Chemicals released by damaged tissues attract white blood cells to the site.
   c. Connective tissue may form a sac around injured tissue and thus block the spread of pathogens.
6. Phagocytosis
   a. The most active phagocytes in blood are neutrophils and monocytes. Monocytes give rise to macrophages, which can remain fixed in tissues.
   b. Phagocytic cells are associated with the linings of blood vessels, in the red bone marrow, liver, spleen, lungs, and lymph nodes.
   c. Phagocytes remove foreign particles from tissues and body fluids.
7. Fever
   Elevated body temperature with the resulting decrease in blood iron level and increase in phagocytic activity hamper infection.

### 14.8 Adaptive (Specific) Defenses, or Immunity (p. 396)

1. Antigens
   a. Before birth, body cells inventory “self” proteins and other large molecules.
   b. After inventory, lymphocytes develop receptors that allow them to differentiate between nonself (foreign) and self antigens.
   c. Haptens are small molecules that can combine with larger ones, becoming antigenic.
2. Lymphocyte origins
   a. Lymphocytes originate in red bone marrow and are released into the blood.
   b. Some reach the thymus, where they mature into T cells.
   c. Others, the B cells, mature in the red bone marrow.
   d. Both T cells and B cells reside in lymphatic tissues and organs.
3. T cells and the cellular immune response
   a. T cells are activated when an antigen-presenting cell displays a foreign antigen.
   b. When a macrophage acts as an accessory cell, it phagocytizes an antigen-bearing agent, digests the agent, and displays the resulting antigens on its cell membrane in association with certain MHC proteins.
   c. T cells respond to antigens by cell-to-cell contact (cellular immune response).
   d. T cells secrete cytokines, such as interleukins, that enhance cellular responses to antigens.
   e. T cells may also secrete substances that are toxic to their target cells.
   f. A helper T cell becomes activated when it encounters displayed antigens for which it is specialized to react.
   g. Once activated, helper T cells stimulate B cells to produce antibodies.
   h. Cytotoxic T cells recognize foreign antigens on tumor cells and cells whose surfaces indicate that they are infected by viruses, then release perforin to destroy these cells.
   i. Memory T cells allow for immediate response to second and subsequent exposure to the same antigen.
4. B cells and the humoral immune response
   a. Sometimes a B cell is activated when it encounters an antigen that fits its antigen receptors or more often a B cell is activated when stimulated by a helper T cell.
   b. An activated B cell proliferates (especially when stimulated by a T cell), enlarging its clone.
   c. Some activated B cells differentiate into antibody-producing plasma cells.
   d. Antibodies react against the antigen-bearing agent that stimulated their production (humoral immune response).
   e. Other activated B cells differentiate further into memory B cells.
   f. An individual’s diverse B cells defend against many pathogens.
5. Types of antibodies
   a. Antibodies are soluble proteins called immunoglobulins.
   b. The five major types of immunoglobulins are IgG, IgA, IgM, IgD, and IgE.
6. Antibody actions
   a. Antibodies directly attach to antigens, activate complement, or stimulate local tissue changes that are unfavorable to antigen-bearing agents.
   b. Direct attachment results in agglutination, precipitation, or neutralization.
   c. Activated complement proteins attract phagocytes, alter cells so that they become more susceptible to phagocytosis, and rupture foreign cell membranes (lysis).
7. Immune responses
   a. The first reaction to an antigen is called a primary immune response.
      (1) During this response, antibodies are produced for several weeks.
      (2) Some T cells and B cells remain dormant as memory cells.
   b. A secondary immune response occurs as a result of memory cells rapidly responding to subsequent exposure to an antigen.
8. Practical classification of immunity
   a. Naturally acquired immunity arises in the course of natural events, whereas artificially acquired immunity is the consequence of a medical procedure.
   b. Active immunity lasts much longer than passive immunity.

   c. A person who encounters a pathogen and has a primary immune response develops naturally acquired active immunity.
   d. A person who receives a vaccine containing a dead or weakened pathogen, or part of one, develops artificially acquired active immunity.
   e. A person who receives an injection of antiserum or gamma globulins has artificially acquired passive immunity.
   f. When antibodies pass through a placental membrane from a pregnant woman to her fetus, the fetus develops naturally acquired passive immunity.
9. Allergic reactions
   a. Allergic reactions are excessive and misdirected immune responses that may damage tissue.
   b. Immediate-reaction allergy is an inborn ability to overproduce IgE.
      (1) Allergic reactions result from mast cells bursting and releasing allergy mediators such as histamine.
      (2) The released chemicals cause allergy symptoms such as hives, hay fever, asthma, eczema, or gastric disturbances.
   c. Delayed-reaction allergy, which can occur in anyone and inflame the skin, results from repeated exposure to antigens.
10. Transplantation and tissue rejection
   a. A transplant recipient's immune system may react against the donated tissue in a tissue rejection reaction.
   b. Matching donor and recipient tissues and using immunosuppressive drugs can minimize tissue rejection.
   c. Immunosuppressive drugs may increase susceptibility to infection.
11. Autoimmunity
   a. In autoimmune disorders, the immune system manufactures autoantibodies that attack a person's own body tissues.
   b. Autoimmune disorders may result from a previous viral infection, faulty T cell development, or reaction to a nonself antigen that resembles a self antigen.

## CHAPTER ASSESSMENTS

### 14.1 Introduction

**1.** Explain the functions of the lymphatic system. (p. 387)

### 14.2 Lymphatic Pathways

**2.** Trace the general pathway of lymph from the interstitial spaces to the bloodstream. (pp. 388–389)

### 14.3 Tissue Fluid and Lymph

**3.** Tissue fluid forms as a result of filtration from blood capillaries exceeding __________________, whereas lymph forms due to increasing __________________ __________________ in the tissue fluid. (p. 390)

**4.** Describe two functions of lymph. (p. 390)

### 14.4 Lymph Movement

**5.** Explain why physical exercise promotes lymphatic circulation. (pp. 390–391)

### 14.5 Lymphatic Tissues and Lymphatic Organs

**6.** Draw a lymph node and label its parts. (p. 391)

**7.** Explain the functions of a lymph node. (p. 392)

**8.** Indicate the locations of the thymus and spleen. (p. 392)

**9.** Compare and contrast the functions of the thymus and spleen. (p. 392)

### 14.6 Body Defenses Against Infection

**10.** Defense mechanisms that prevent the entry of many types of pathogens and destroy them if they enter provide __________ (nonspecific) defense. Precise mechanisms targeting specific pathogens provide ___________ (specific) defense. (p. 394)

### 14.7 Innate (Nonspecific) Defenses

**11.** Define *species resistance.* (p. 394)

**12.** Identify the barriers that provide the body's first line of defense against infectious agents. (p. 394)

**13.** Describe how enzymatic actions function as defense mechanisms. (p. 395)

**14.** Define *interferon,* and explain its action. (p. 395)

**15.** ___________ is a group of plasma proteins that when activated stimulate inflammation, attract phagocytes, and enhance phagocytosis. (p. 395)

**16.** _________ _________ _________ are specialized lymphocytes that secrete perforins to lyse cell membranes of virus-infected cells. (p. 395)

**17.** List the major effects of inflammation, and explain why each occurs. (p. 395)

**18.** Identify the major phagocytic cells in blood and other tissues. (p. 395)

**19.** Discuss why low-grade fever of short duration may be a desired response to infection. (p. 395)

### 14.8 Adaptive (Specific) Defenses, or Immunity

**20.** Review the origin of T cells and B cells. (p. 396)

**21.** Explain the cellular immune response including the activation of T cells. (pp. 396–397)

**22.** List three types of T cells, and describe the function of each in the immune response. (p. 398)

**23.** Explain the humoral immune response, including the activation of B cells. (pp. 399–400)

**24.** Explain the function of plasma cells. (p. 400)

**25.** Match the major types of antibodies with their function and/or where each is found. (p. 401)

(1) associated with allergic reactions
(2) important in B cell activation, on surfaces of most B cells
(3) activates complement, anti-A and anti-B in blood
(4) effective against bacteria, viruses, toxins in plasma and tissue fluids
(5) found in exocrine secretions, including breast milk

A. IgA
B. IgM
C. IgG
D. IgD
E. IgE

**26.** Describe three ways in which an antibody's direct attack on an antigen helps remove that antigen. (p. 401)

**27.** List the various effects of complement activation. (p. 401)

**28.** Contrast a primary and a secondary immune response. (p. 402)

**29.** Match the practical classification of immunity with its example. (p. 402)

(1) naturally acquired active immunity
(2) artificially acquired active immunity
(3) naturally acquired passive immunity
(4) artificially acquired passive immunity

A. a breast-fed newborn
B. gamma globulin injection
C. vaccination
D. measles infection

**30.** Describe how an immediate-reaction allergic response may occur. (p. 403)

**31.** List the major events leading to a delayed-reaction allergic response. (p. 404)

**32.** Explain the relationship between tissue rejection and an immune response. (p. 404)

**33.** Explain the relationship between autoimmunity and an immune response. (p. 404)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 6.2, 14.2, 14.3, 14.4

**1.** Why is injecting a substance into the skin like injecting it into the lymphatic system?

### OUTCOMES 14.2, 14.3, 14.4, 14.5

**2.** How can the removal of enlarged lymph nodes for microscopic examination aid in diagnosing certain diseases?

### OUTCOME 14.8

**3.** The immune response is specific, diverse, and has memory. Give examples of each of these characteristics.

**4.** Some parents keep their preschoolers away from other children to prevent them from catching illnesses. How might these well-meaning parents actually be harming their children?

**5.** Why does vaccination provide long-lasting protection against a disease, while gamma globulin (IgG) provides only short-term protection?

**6.** Why is a transplant consisting of fetal tissue less likely to provoke an immune rejection response than tissue from an adult?

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# 15

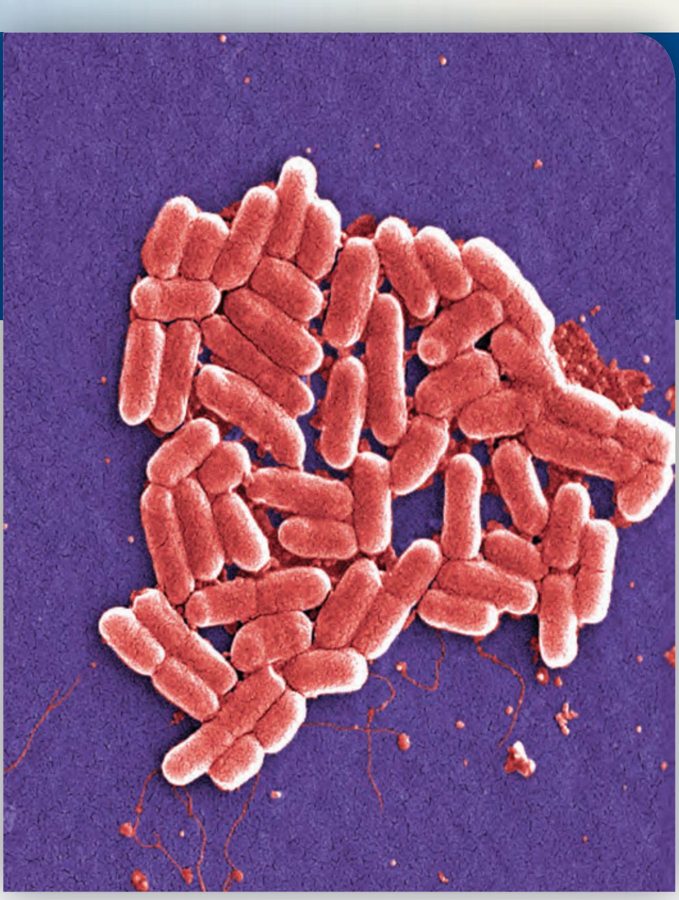
# Digestive System and Nutrition

The gut microbiome. Not all of the cells in an adult body are human—90% are microorganisms traditionally called microflora, but more recently called the *microbiome*. The "human oral microbiome," for example, includes more than 600 species that can live in the mouth. Each person has about 200 of these oral bacterial types. The other end of the digestive tract houses the "distal gut microbiome," which includes more than 6,800 species.

Researchers tracked the formation and changing nature of the human gut microbiome by classifying microbial DNA in a year's worth of stool collected daily from soiled diapers. Bacteria in the stool varied greatly from baby to baby at the onset, but by the babies' first birthdays, the gut communities were more alike and more closely resembled the microbial communities in adults.

The microorganisms that live in our large intestines are crucial to our health. They produce more than eighty types of enzymes that digest plant polysaccharides that our bodies cannot break down, and help process certain sugars. Our "gut" residents also synthesize vitamins and amino acids, and break down certain toxins and drugs.

We can use knowledge of our gut microbiome to improve health, because illness can alter the bacterial populations within us. A new focus on drug development is to target our microbial residents. An approach called probiotics adds bacteria to foods to prevent certain infections. For example, certain *Lactobacillus* strains added to yogurt help protect against *Salmonella* food-borne infection.



*Several million microorganisms are normal residents of our digestive tracts.* Escherichia coli, *pictured here (6,800×), produce vitamin K and if present in low numbers, will not cause diarrhea.*

A very old treatment is based on restoring a gut microbiome altered by disease. In a procedure called fecal microbiota transplantation, people with recurrent infection from *Clostridium difficile*, which causes severe diarrhea, receive feces from a healthy donor, which reconstitutes a healthy gut microbiome. This procedure has been performed by enema in cattle for a century, and since 1958 in humans. A recent clinical trial introduced the fecal material via a tube through the nose to the small intestine. Techniques that detect bacterial genomes reveal that the treatment can indeed restore the healthy small intestine's microbiome.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 15.1 Introduction

1. Describe the general functions of the digestive system. (p. 411)
2. Name the major organs of the digestive system. (p. 411)

### 15.2 General Characteristics of the Alimentary Canal

3. Describe the structure of the wall of the alimentary canal. (pp. 411–413)
4. Explain how the contents of the alimentary canal are mixed and moved. (p. 413)

### 15.3 Mouth

5. Describe the functions of the structures associated with the mouth. (pp. 413–414)
6. Describe how different types of teeth are adapted for different functions, and list the parts of a tooth. (p. 417)

### 15.4–15.10 Salivary Glands–Large Intestine

7. Locate each of the digestive organs and glands; then describe the general function of each. (pp. 418–437)
8. Identify the function of each enzyme secreted by the digestive organs. (pp. 418–432)
9. Describe how digestive secretions are regulated. (pp. 418–432)
10. Describe the mechanisms of swallowing and defecating. (pp. 419–437)
11. Explain how the products of digestion are absorbed. (p. 433)

Anatomy & Physiology REVEALED apr.revealed.com **Module 12** Digestive System

**15.11 Nutrition and Nutrients**

**12.** List the major sources of carbohydrates, lipids, and proteins. (pp. 438–441)

**13.** Describe how cells use carbohydrates, lipids, and proteins. (pp. 439–441)

**14.** Identify the functions of each fat-soluble and water-soluble vitamin. (pp. 442–443)

**15.** Identify the functions of each major mineral and trace element. (pp. 444 and 446)

**16.** Describe an adequate diet. (p. 444)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**aliment-** [food] *aliment*ary canal: Tubelike part of the digestive system.

**chym-** [juice] *chym*e: Semifluid paste of food particles and gastric juice formed in the stomach.

**decidu-** [falling off] *decidu*ous teeth: Teeth shed during childhood.

**gastr-** [stomach] *gastr*ic gland: Part of the stomach that secretes gastric juice.

**hepat-** [liver] *hepat*ic duct: Duct that carries bile from the liver to the bile duct.

**lingu-** [tongue] *lingu*al tonsil: Mass of lymphatic tissue at the root of the tongue.

**nutri-** [nourish] *nutri*ent: Substance needed to nourish cells.

**peri-** [around] *peri*stalsis: Wavelike ring of contraction that moves material along the alimentary canal.

**pyl-** [gatekeeper] *pyl*oric sphincter: Muscle that serves as a valve between the stomach and small intestine.

**vill-** [hairy] *vill*i: Tiny projections of mucous membrane in the small intestine.

## 15.1 | Introduction

**Digestion** (di-jest′yun) is the mechanical and chemical breakdown of foods and the absorption of the resulting nutrients by cells. *Mechanical digestion* breaks large pieces into smaller ones without altering their chemical composition. *Chemical digestion* breaks food into simpler chemicals. The organs of the **digestive system** carry out these processes.

The digestive system consists of the **alimentary canal** (al″i-men′tar-e kah-nal′), extending from the mouth to the anus, and several accessory organs, which secrete substances, into the canal, used in digestion. The alimentary canal includes the mouth, pharynx, esophagus, stomach, small intestine, large intestine, rectum, and anus; the accessory organs include the salivary glands, liver, gallbladder, and pancreas (fig. 15.1; see reference plates 4, 5, and 6, pp. 35–37). Overall, the digestive system is a tube, open at both ends, that has a surface area of 186 square meters. It supplies nutrients for body cells.

**PRACTICE**

1. What are the general functions of the digestive system?
2. Which organs constitute the digestive system?

## 15.2 | General Characteristics of the Alimentary Canal

The alimentary canal is a muscular tube about 8 meters long that passes through the body's thoracic and abdominopelvic cavities (fig. 15.2). The structure of its wall, how it moves food, and its innervation are similar throughout its length.

### Structure of the Wall

The wall of the alimentary canal consists of four distinct layers that are developed to different degrees from region to region. Although the four-layered structure persists throughout the alimentary canal, certain regions are

**CAREER CORNER**

### Registered Dietitian

In preparation for weight-loss surgery, the young woman must lose 10% of her body weight. A registered dietitian (RD) assists by discussing the types of foods that an obese person with type 2 diabetes mellitus should and shouldn't eat. The RD uses plastic models of foods to demonstrate the makeup of appropriate meals, and then works with the patient to develop a meal plan.

Dietitians work in diverse settings. These include businesses, hotels, food service corporations, community agencies, schools, senior centers, health-care facilities, prisons, and restaurants. Registered dietitians can also have careers in research or teaching other health-care professionals, or open their own businesses. Educating the public about healthful food choices can be a major part of the job.

Training to become a registered dietitian includes earning a bachelor's degree in an accredited program, completing a supervised practice program typically lasting 6 to 12 months, passing a national exam, and taking continuing education courses.

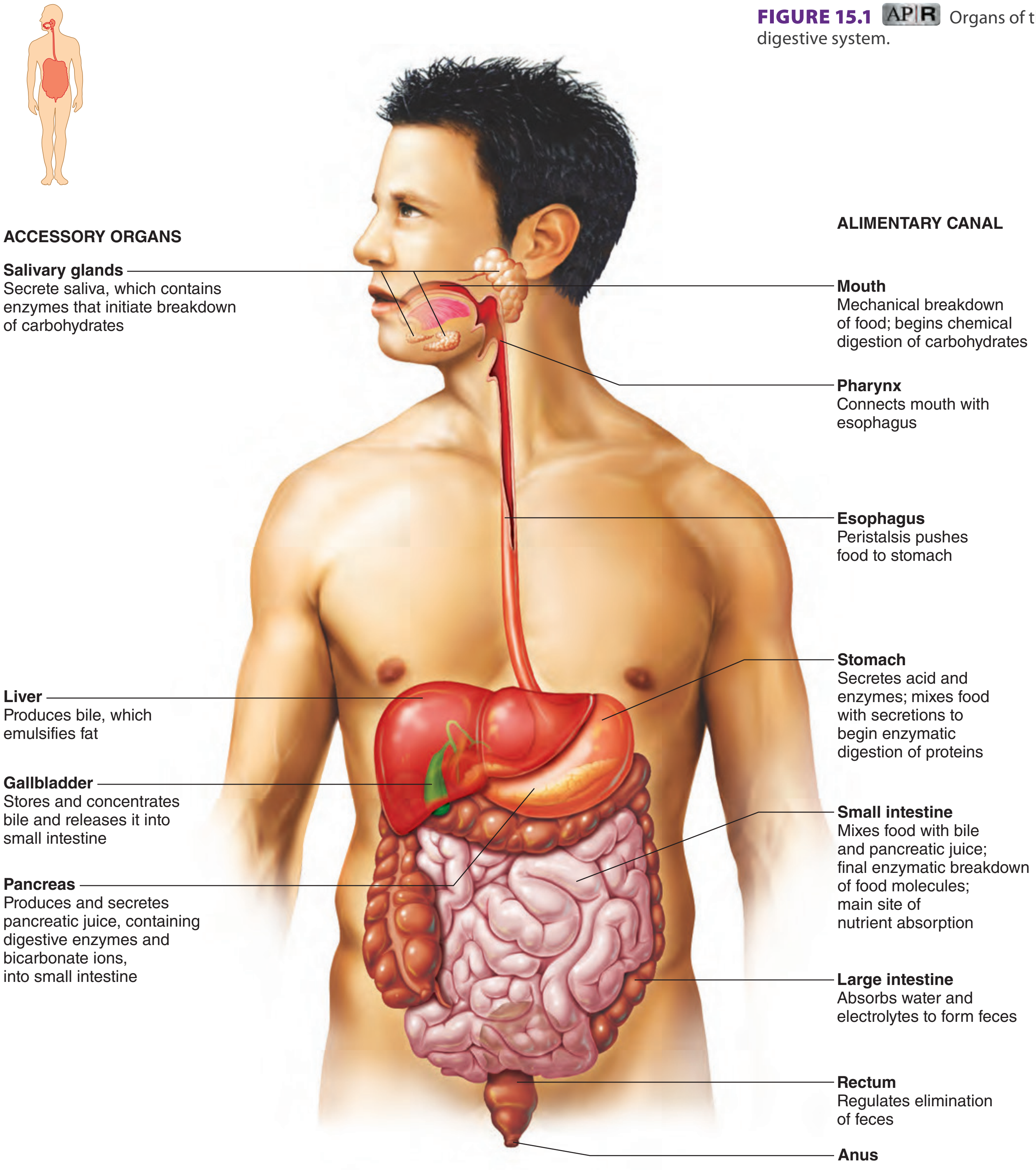

ACCESSORY ORGANS
Salivary glands
Secrete saliva, which contains enzymes that initiate breakdown of carbohydrates
Liver
Produces bile, which emulsifies fat
Gallbladder
Stores and concentrates bile and releases it into small intestine
Pancreas
Produces and secretes pancreatic juice, containing digestive enzymes and bicarbonate ions, into small intestine
ALIMENTARY CANAL
Mouth
Mechanical breakdown of food; begins chemical digestion of carbohydrates
Pharynx
Connects mouth with esophagus
Esophagus
Peristalsis pushes food to stomach
Stomach
Secretes acid and enzymes; mixes food with secretions to begin enzymatic digestion of proteins
Small intestine
Mixes food with bile and pancreatic juice; final enzymatic breakdown of food molecules; main site of nutrient absorption
Large intestine
Absorbs water and electrolytes to form feces
Rectum
Regulates elimination of feces
Anus

**FIGURE 15.1** APR Organs of the digestive system.

specialized for particular functions. Beginning with the innermost tissues, these layers are (fig. 15.3):

1. **Mucosa** (mu-ko′sah), or **mucous membrane** (mu′kus mem′brān) Surface epithelium, underlying connective tissue, and a small amount of smooth muscle form this layer. In some regions, the mucosa is folded, with tiny projections that extend into the passageway, or **lumen** (lu′men), of the digestive tube. The folds increase the absorptive surface area. The mucosa also has glands that are tubular invaginations into which the lining cells secrete mucus and digestive enzymes. The mucosa protects the tissues beneath it and carries on secretion and absorption.

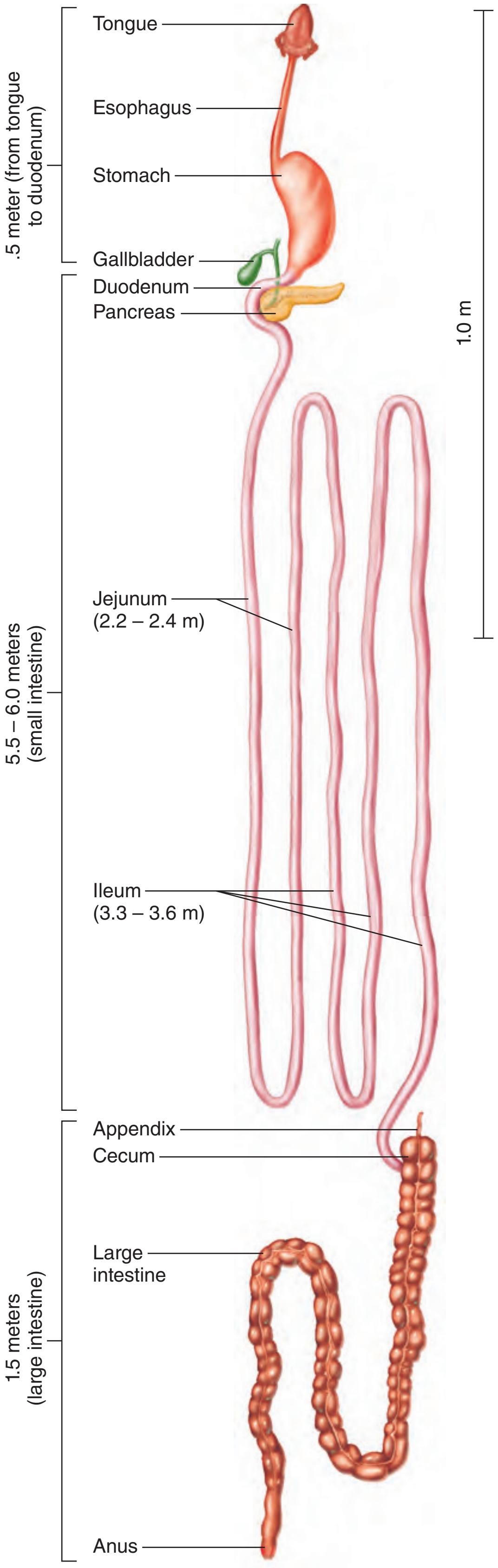


**FIGURE 15.2** The alimentary canal is a muscular tube about 8 meters long.

**Q** *What is the distance from the tongue to the duodenum in English units (inches).*

**Answer can be found in Appendix F on page 582.**

2. **Submucosa** (sub″mu-ko′sah) The submucosa contains considerable loose connective tissue as well as glands, blood vessels, lymphatic vessels, and nerves. Its vessels nourish surrounding tissues and carry away absorbed materials.
3. **Muscular layer** This layer, which provides movements of the tube, consists of two coats of smooth muscle tissue. The fibers of the inner coat encircle the tube. When these *circular fibers* contract, the tube's diameter decreases. The fibers of the outer muscular coat run lengthwise. When these *longitudinal fibers* contract, the tube shortens.
4. **Serosa** (sĕ′ro-sah), or **serous layer** (se′rus la′er) The layer of epithelium on the outside and the connective tissue beneath compose the serous layer, or outer covering, of the tube, also called the *visceral peritoneum*. The cells of the serosa protect underlying tissues and secrete serous fluid, which moistens and lubricates the tube's outer surface so that organs within the abdominal cavity slide freely against one another.

## Movements of the Tube

The motor functions of the alimentary canal are of two basic types—*mixing movements* and *propelling movements*. Mixing occurs when smooth muscles in small segments of the tube contract rhythmically (fig. 15.4*a*). For example, when the stomach is full, waves of muscular contractions move along its walls from one end to the other. These waves mix food with digestive juices that the mucosa secretes. In the small intestine, a process called **segmentation** aids mixing by alternately contracting and relaxing the smooth muscle in nonadjacent segments of the organ. Because segmentation follows a back and forth pattern, materials are not moved along the tract in one direction (fig. 15.4*b*).

Propelling movements include a wavelike motion called **peristalsis** (per″ĭ-stal′sis). In peristalsis, a ring of contraction occurs in the wall of the tube. At the same time, the muscular wall just ahead of the ring relaxes. As the peristaltic wave moves along the tube, it pushes the tubular contents ahead of it (fig. 15.4*c*).

**PRACTICE**

3. Describe the wall of the alimentary canal.
4. Name the two basic types of movements in the alimentary canal.

## 15.3 | Mouth

The **mouth** receives food and begins digestion by mechanically breaking up solid particles into smaller pieces and mixing them with saliva. This action is called

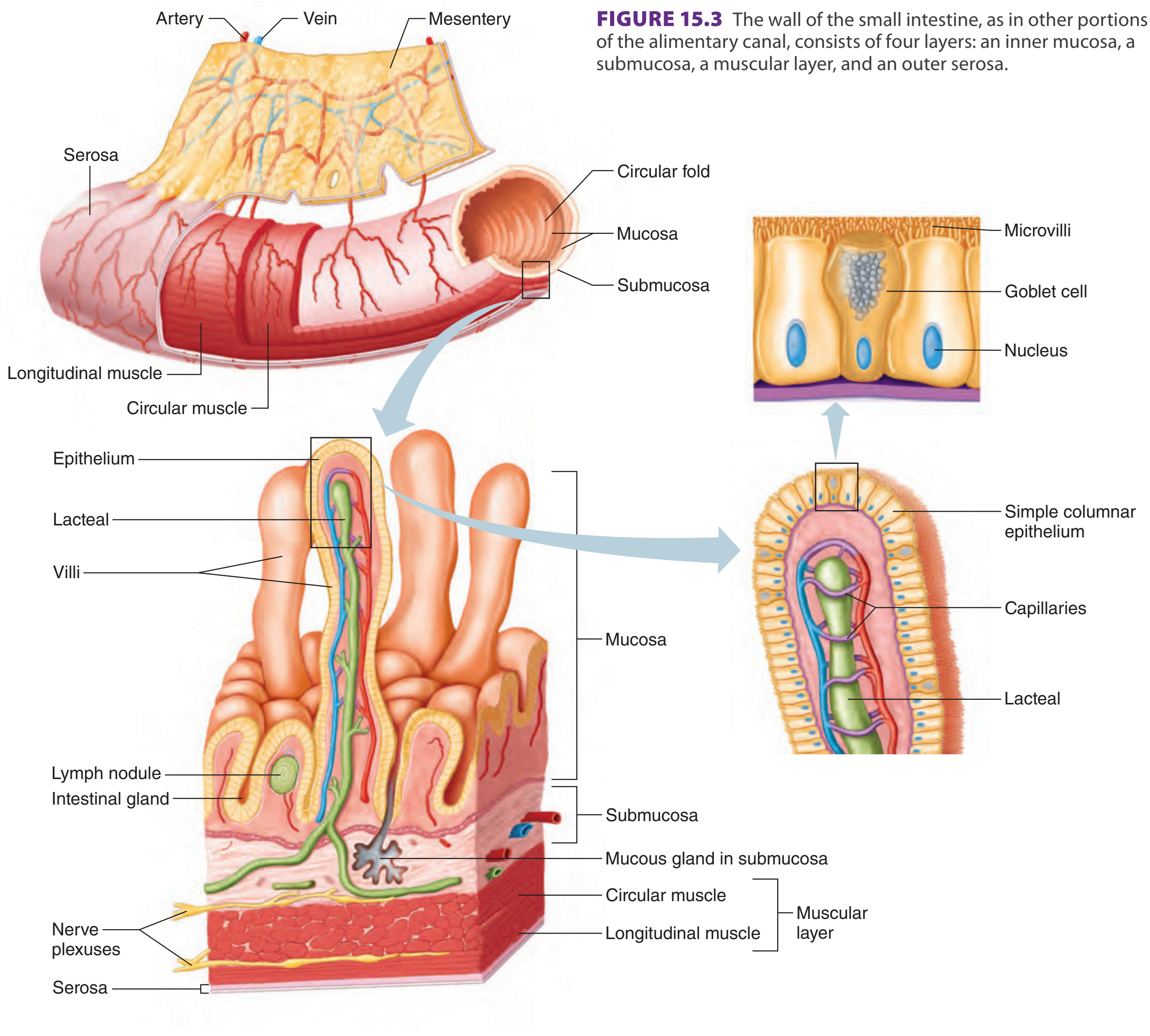

Artery
Vein
Mesentery
Serosa
Circular fold
Mucosa
Submucosa
Longitudinal muscle
Circular muscle
Microvilli
Goblet cell
Nucleus
Epithelium
Lacteal
Villi
Simple columnar epithelium
Capillaries
Lacteal
Mucosa
Lymph nodule
Intestinal gland
Submucosa
Mucous gland in submucosa
Circular muscle
Longitudinal muscle
Muscular layer
Nerve plexuses
Serosa

**FIGURE 15.3** The wall of the small intestine, as in other portions of the alimentary canal, consists of four layers: an inner mucosa, a submucosa, a muscular layer, and an outer serosa.

*mastication* (mas″tĭ-ka′shun). The lips, cheeks, tongue, and palate surround the mouth, which includes a chamber between the palate and tongue called the *oral cavity,* as well as a narrow space between the teeth, cheeks, and lips called the *vestibule* (fig. 15.5).

## Cheeks and Lips

The **cheeks,** forming the lateral walls of the mouth, consist of outer layers of skin, pads of subcutaneous fat, muscles associated with expression and chewing, and inner linings of moist, stratified squamous epithelium. The **lips** are highly mobile structures that surround the mouth opening. They contain skeletal muscles and sensory receptors useful in judging the temperature and texture of foods. Blood vessels near lip surfaces impart a reddish color.

## Tongue

The **tongue** nearly fills the oral cavity when the mouth is closed. Mucous membrane covers the tongue, and a membranous fold called the **lingual frenulum** (ling′gwahl fren′u-lum) connects the midline of the tongue to the floor of the mouth.

The *body* of the tongue is mostly skeletal muscle. Muscular action mixes food particles with saliva during chewing and moves food toward the pharynx during swallowing. The tongue also helps move food underneath the teeth for chewing. Rough projections called **papillae** on the tongue surface provide friction, which helps handle food. These papillae also bear taste buds (see chapter 10, p. 280).

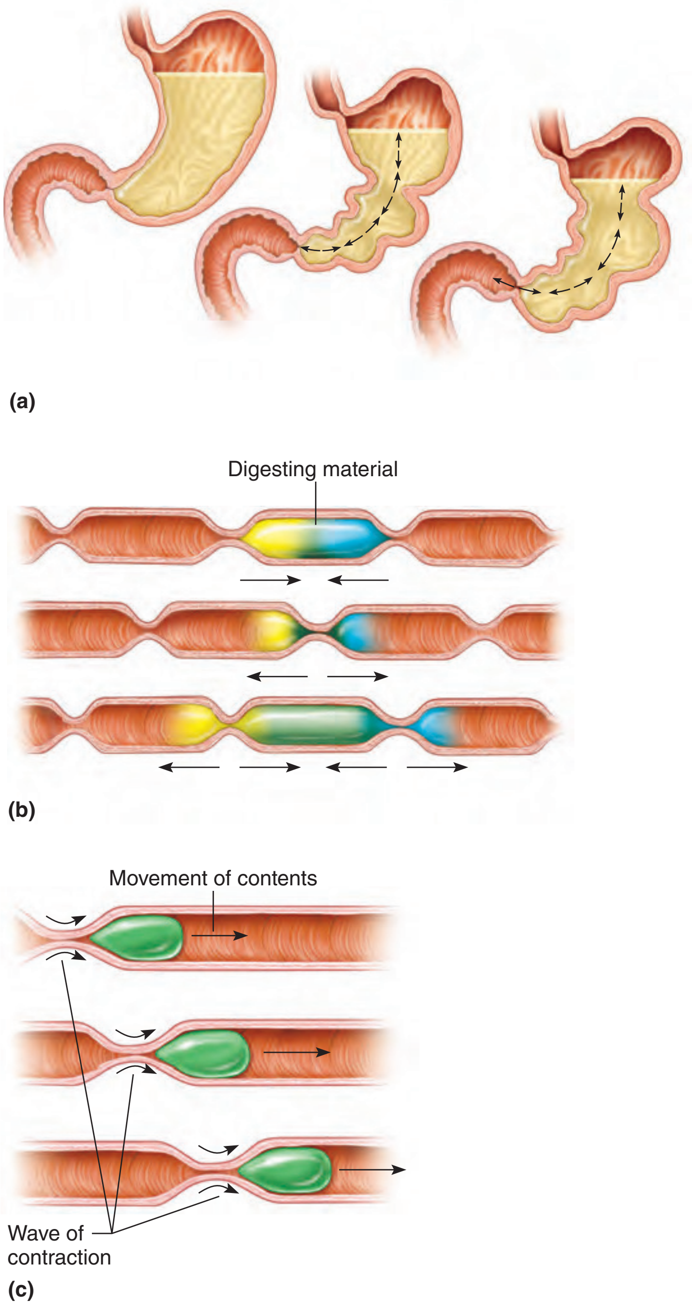


**FIGURE 15.4** Movements through the alimentary canal. (**a**) Mixing movements occur when small segments of the muscular wall of the stomach rhythmically contract. (**b**) Segmentation mixes contents of the small intestine. (**c**) Peristaltic waves move the contents along the canal.

The posterior region, or *root,* of the tongue is anchored to the hyoid bone. It is covered with rounded masses of lymphatic tissue called **lingual tonsils** (ton′silz) (fig. 15.6).

## Palate

The **palate** (pal′at) forms the roof of the oral cavity and consists of a bony anterior part (*hard palate*) and a muscular posterior part (*soft palate*). A muscular arch of the soft palate extends posteriorly and downward as a cone-shaped projection called the **uvula** (u′vu-lah).

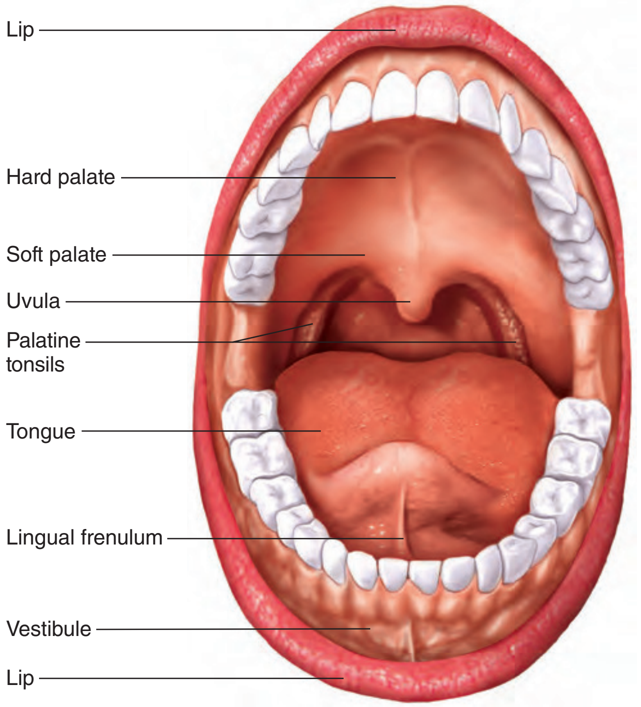


**FIGURE 15.5** The mouth is adapted for ingesting food and beginning digestion, both mechanically and chemically.

In the back of the mouth, on either side of the tongue and closely associated with the palate, are masses of lymphatic tissue called **palatine** (pal′ah-tīn) **tonsils** (see figs. 15.5 and 15.6). These structures lie beneath the epithelial lining of the mouth and, like other lymphatic tissues, help protect the body against infection.

The palatine tonsils are common sites of infection, and become inflamed in *tonsillitis*. Infected tonsils may swell so greatly that they block the passageways of the pharynx and interfere with breathing and swallowing. When tonsillitis recurs and does not respond to antibiotic treatment, the tonsils may be surgically removed. Such tonsillectomies are done less often today than they were a generation ago because the tonsils' role in immunity is now recognized.

Other masses of lymphatic tissue, called **pharyngeal** (fah-rin′je-al) **tonsils,** or *adenoids,* are on the posterior wall of the pharynx, above the border of the soft palate (fig. 15.6). Enlarged adenoids that block the passage between the nasal cavity and the pharynx may be surgically removed.

## PRACTICE

5. How does the tongue function as part of the digestive system?
6. Where are the tonsils located?

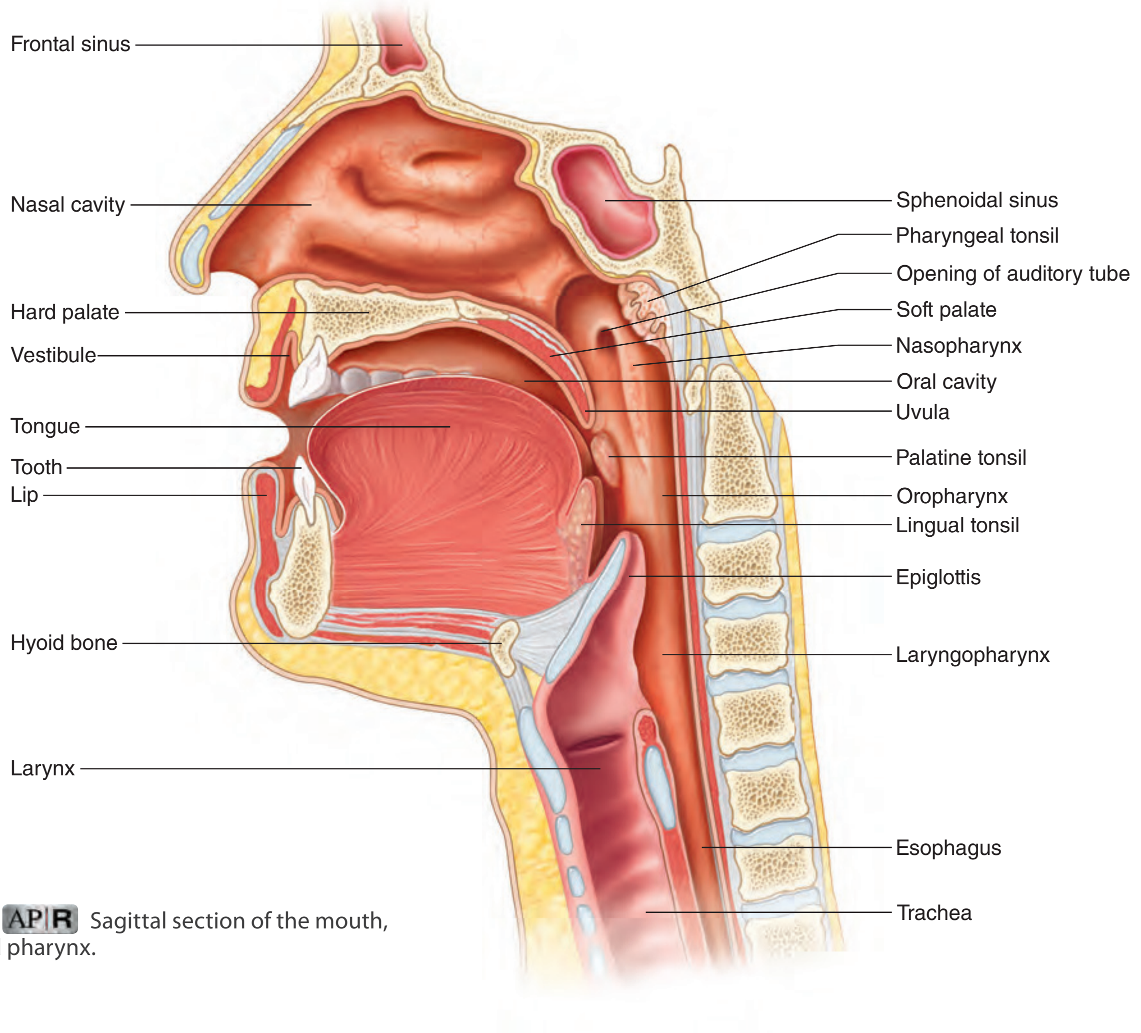

Frontal sinus
Nasal cavity
Hard palate
Vestibule
Tongue
Tooth
Lip
Hyoid bone
Larynx
Sphenoidal sinus
Pharyngeal tonsil
Opening of auditory tube
Soft palate
Nasopharynx
Oral cavity
Uvula
Palatine tonsil
Oropharynx
Lingual tonsil
Epiglottis
Laryngopharynx
Esophagus
Trachea

**FIGURE 15.6** APR Sagittal section of the mouth, nasal cavity, and pharynx.

## Teeth

Two different sets of **teeth** form during development. The first set, the *primary teeth* (deciduous teeth), usually erupt through the gums (gingiva) at regular intervals between the ages of six months and two to four years (fig. 15.7). There are twenty deciduous teeth—ten in each jaw.

The primary teeth are usually shed in the same order they erupted. After their roots are resorbed, the *secondary teeth* (permanent teeth) push the primary teeth out of their sockets. This secondary set consists of thirty-two teeth—sixteen in each jaw (fig. 15.8). The secondary teeth usually begin to erupt at six years, but the set may not be complete until the third molars (wisdom teeth) emerge between seventeen and twenty-five years.

Teeth begin mechanical digestion by breaking pieces of food into smaller pieces. This action increases the surface area of food particles, allowing more digestive enzyme access to the food molecules. Table 15.1 summarizes the number and types of teeth that appear during development and their functions.

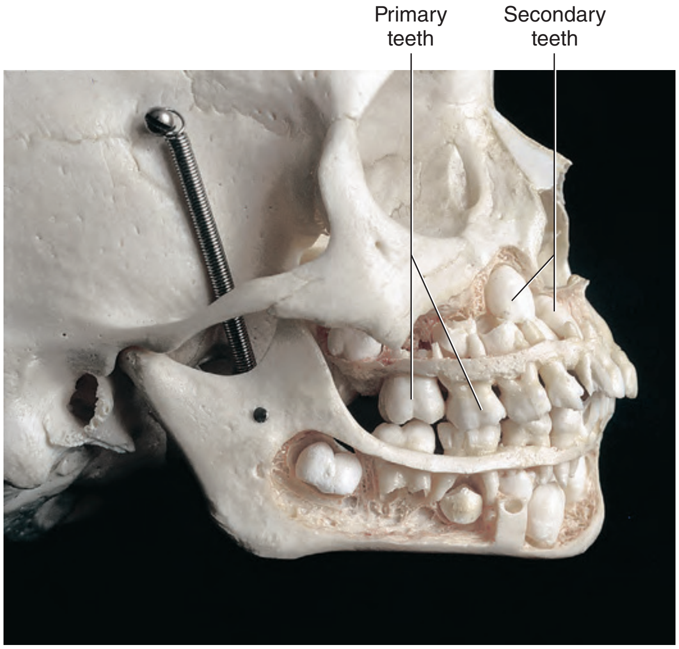

Primary teeth
Secondary teeth

**FIGURE 15.7** This partially dissected child's skull reveals primary and developing secondary teeth in the maxilla and mandible.

**TABLE 15.1 Primary and Secondary Teeth**

| Type | Number of Primary Teeth | Number of Secondary Teeth | Function |
|---|---|---|---|
| Incisor | | | Bite off pieces of food |
| Central | 4 | 4 | |
| Lateral | 4 | 4 | |
| Canine (cuspid) | 4 | 4 | Grasp and tear food |
| Premolar (bicuspid) | | | Grind food particles |
| First | 0 | 4 | |
| Second | 0 | 4 | |
| Molar | | | Grind food particles |
| First | 4 | 4 | |
| Second | 4 | 4 | |
| Third | 0 | 4 | |
| Total | 20 | 32 | |

Each tooth consists of two main parts—the *crown,* which projects beyond the gum, and the *root,* which is anchored to the alveolar process of the jaw. These structures meet at the *neck* of the tooth.

Glossy white *enamel* covers the crown. Enamel mainly consists of calcium salts and is the hardest substance in the body. Enamel damaged by abrasive action or injury is not replaced. Enamel also tends to wear away with age. Clinical Application 15.1 discusses tooth enamel destruction.

The bulk of a tooth beneath the enamel is *dentin,* a substance much like bone but harder. Dentin surrounds the tooth's central cavity (pulp cavity), which contains blood vessels, nerves, and connective tissue, collectively called *pulp.* Blood vessels and nerves reach this cavity through tubular *root canals*, which extend into the root.

A thin layer of bonelike material called *cementum,* surrounded by a *periodontal ligament,* encloses the root. This ligament contains blood vessels and nerves as well as bundles of thick collagen fibers that pass between the cementum and the bone of the alveolar process, firmly attaching the tooth to the jaw (fig. 15.9).

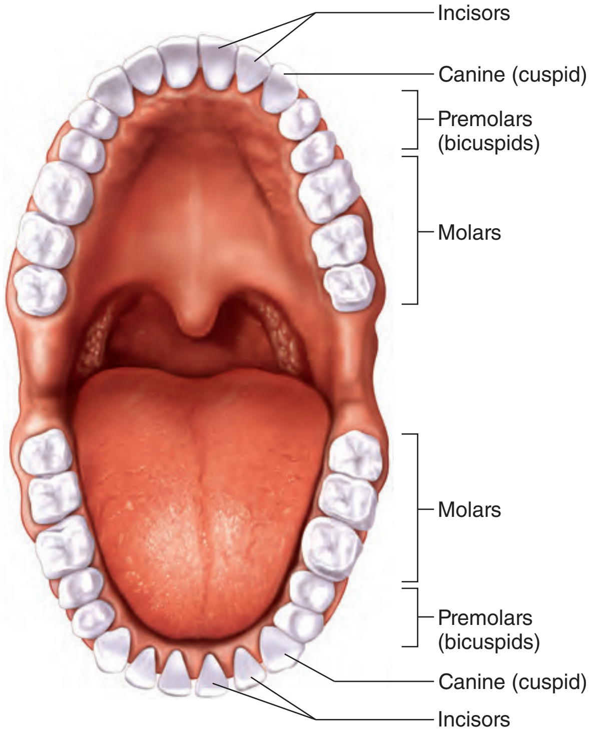

Incisors
Canine (cuspid)
Premolars (bicuspids)
Molars
Molars
Premolars (bicuspids)
Canine (cuspid)
Incisors

**FIGURE 15.8** APR The secondary teeth of the upper and lower jaws.

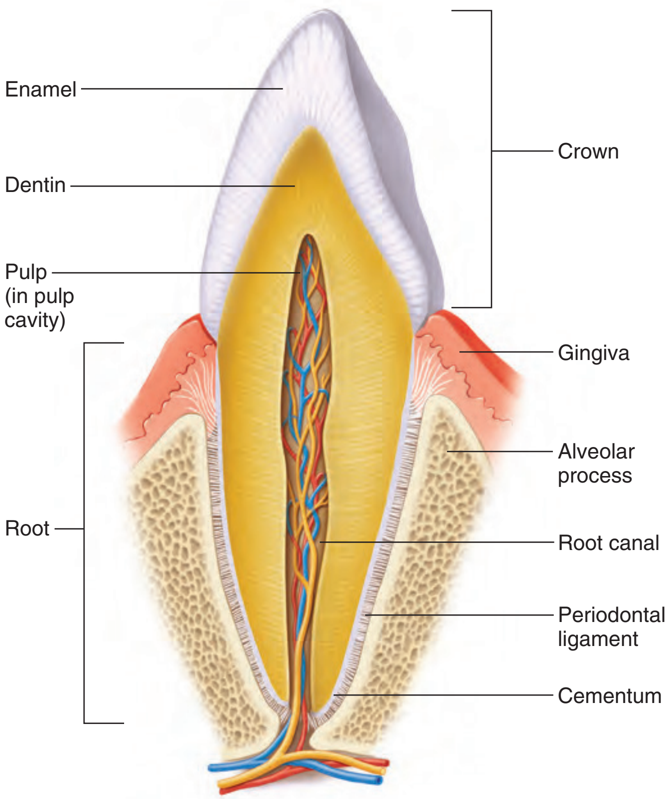

Enamel
Dentin
Pulp (in pulp cavity)
Root
Crown
Gingiva
Alveolar process
Root canal
Periodontal ligament
Cementum

**FIGURE 15.9** A section of a tooth.

## CLINICAL APPLICATION 15.1

### Dental Caries

Sticky foods, such as caramel, lodge between the teeth and in the crevices of molars, feeding bacteria such as *Actinomyces, Streptococcus mutans,* and *Lactobacillus.* These microorganisms metabolize carbohydrates in the food, producing acid by-products that destroy tooth enamel and dentin. The bacteria also produce sticky substances that hold them in place.

If a person eats a candy bar but does not brush the teeth soon afterward, the acid-forming bacteria may cause tooth decay, creating a condition called *dental caries.* Unless a dentist cleans and fills the resulting cavity that forms where enamel is destroyed, the damage will spread to the underlying dentin.

The following may help prevent dental caries:

1. Brush and floss teeth regularly.
2. Have regular dental exams and cleanings.
3. Talk with your dentist about receiving a fluoride treatment. Fluoride is added to the water supply in many communities. Fluoride is incorporated into the enamel's chemical structure, strengthening it.
4. The dentist may apply a sealant to children's and adolescents' teeth where crevices might hold onto decay-causing bacteria. The sealant is a coating that keeps acids from eating away at tooth enamel.

### PRACTICE

7. How do primary teeth differ from secondary teeth?
8. Describe the structure of a tooth.
9. Explain how a tooth is attached to the bone of the jaw.

## 15.4 | Salivary Glands

The **salivary** (sal′ī-ver-e) **glands** secrete *saliva.* This fluid moistens food particles, helps bind them, and begins the chemical digestion of carbohydrates. Saliva is also a solvent, dissolving foods so that they can be tasted, and it helps cleanse the mouth and teeth.

### Salivary Secretions

A salivary gland has two types of secretory cells—*serous cells* and *mucous cells.* Proportions of these cells vary in the different types of salivary glands. Serous cells produce a watery fluid that contains the digestive enzyme **salivary amylase** (am′ĭ-lās). This enzyme splits starch and glycogen molecules into disaccharides—the first step in the chemical digestion of carbohydrates. Mucous cells secrete a thick liquid called **mucus,** which binds food particles and acts as a lubricant during swallowing.

When a person sees, smells, tastes, or even thinks about appealing food, parasympathetic impulses elicit the secretion of a large volume of watery saliva. Conversely, food that looks, smells, or tastes unpleasant inhibits parasympathetic activity and less saliva is produced. Swallowing may become difficult.

### Major Salivary Glands

Three pairs of major salivary glands—the parotid, submandibular, and sublingual glands—and many minor ones are associated with the mucous membranes of the tongue, palate, and cheeks (fig. 15.10). The **parotid glands** (pah-rot′id glandz) are the largest of the major salivary glands. Each gland lies anterior and somewhat inferior to each ear, between the skin of the cheek and the masseter muscle. The parotid gland secretory cells are primarily serous cells. These glands secrete a clear, watery fluid that is rich in salivary amylase.

The **submandibular** (sub″man-dib′u-lar) **glands** are located in the floor of the mouth on the inside surface of the lower jaw. The secretory cells of these glands are about equally serous and mucous. Consequently, the submandibular glands secrete a more viscous fluid than the parotid glands.

The **sublingual** (sub-ling′gwal) **glands,** the smallest of the major salivary glands, are on the floor of the mouth inferior to the tongue. Their secretory cells are primarily the mucous type, making their secretions thick and stringy.

### PRACTICE

10. What is the function of saliva?
11. What stimulates salivary glands to secrete saliva?
12. Where are the major salivary glands located?

## 15.5 | Pharynx and Esophagus

The pharynx is a cavity posterior to the mouth from which the tubular esophagus leads to the stomach (see fig. 15.1). The pharynx and the esophagus do not digest food, but both are important passageways and their muscular walls function in swallowing.

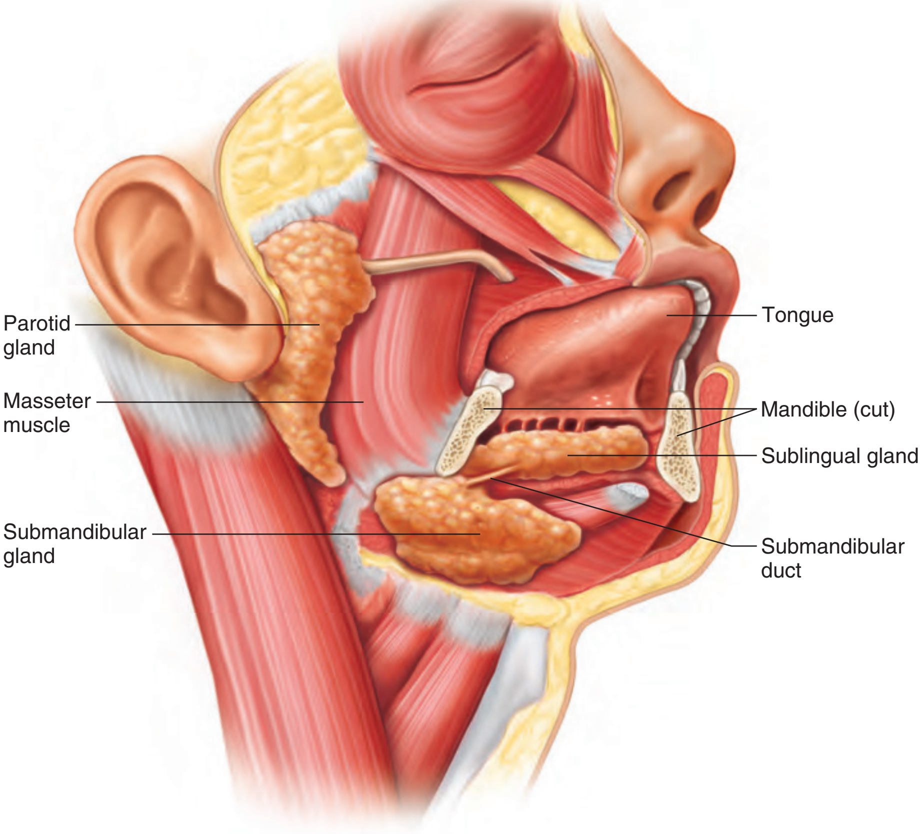


**FIGURE 15.10** APR Locations of the major salivary glands.

## Structure of the Pharynx

The **pharynx** (far′inks) connects the nasal and oral cavities with the larynx and esophagus (see fig. 15.6). It has three parts:

1. The **nasopharynx** (na″zo-far′inks) communicates with the nasal cavity and provides a passageway for air during breathing. The auditory tubes, which connect the pharynx with the middle ears, open through the walls of the nasopharynx.
2. The **oropharynx** (o″ro-far′inks) is posterior to the soft palate and inferior to the nasopharynx. It is a passageway for food moving downward from the mouth and for air moving to and from the nasal cavity.
3. The **laryngopharynx** (lah-ring″go-far′inks), just inferior to the oropharynx, is a passageway to the esophagus.

## Swallowing Mechanism

Swallowing has three stages. In the first stage, which is voluntary, food is chewed and mixed with saliva. Then the tongue rolls this mixture into a mass, or **bolus,** and forces it into the oropharynx.

The second stage of swallowing begins as food reaches the oropharynx and stimulates sensory receptors around the pharyngeal opening. This triggers the swallowing reflex, which includes the following actions:

1. The soft palate (including the uvula) raises, preventing food from entering the nasal cavity.
2. The hyoid bone and the larynx are elevated. A flaplike structure attached to the larynx, called the *epiglottis* (ep″ĭ-glot′is), closes off the top of the larynx so that food is less likely to enter the trachea.
3. The tongue is pressed against the soft palate, sealing off the oral cavity from the nasopharynx.
4. The longitudinal muscles in the pharyngeal wall contract, pulling the pharynx upward toward the food.
5. Muscles in the laryngopharynx relax, opening the esophagus.
6. A peristaltic wave begins in the pharyngeal muscles and forces food into the esophagus.

The swallowing reflex momentarily inhibits breathing. Then, during the third stage of swallowing, peristalsis transports the food in the esophagus to the stomach.

**FACTS OF LIFE** Computer simulation studies show that each type of food requires an optimum range of number of chews to form a bolus. Eating raw carrots, for example, requires twenty to twenty-five chews.

## Esophagus

The **esophagus** (ĕ-sof′ah-gus), a straight, collapsible tube about 25 centimeters long, is a food passageway from the pharynx to the stomach (see figs. 15.1 and 15.6). The esophagus begins at the base of the laryngopharynx and descends posterior to the trachea, passing through the mediastinum. It penetrates the diaphragm through an opening, the *esophageal hiatus* (ĕ-sof″ah-je′al hi-a′tus), and is continuous with the stomach on the abdominal side of the diaphragm.

Mucous glands are scattered throughout the submucosa of the esophagus. Their secretions moisten and lubricate the tube's inner lining.

Just superior to the point where the esophagus joins the stomach, some of the circular smooth muscle fibers have increased muscle tone, forming the **lower esophageal sphincter** (loh′er ĕ-sof″ah-je′al sfingk′ter), or cardiac sphincter (fig. 15.11). These fibers usually remain contracted. They close the entrance to the stomach, preventing the stomach contents from regurgitating into the esophagus. When peristaltic waves reach the stomach, these muscle fibers temporarily relax and allow the swallowed food to enter.

In a *hiatal hernia,* part of the stomach protrudes through a weakened area of the diaphragm, through the esophageal hiatus, and into the thorax. Regurgitation (reflux) of gastric juice into the esophagus becomes more likely. This may inflame the esophageal mucosa, causing a burning sensation (heartburn), difficulty in swallowing, or ulceration and blood loss. In response to the destructive action of gastric juice, columnar epithelium may replace the squamous epithelium that normally lines the esophagus (see chapter 5, pages 108–109). This condition, called *Barrett's esophagus,* increases the risk of developing esophageal cancer.

### PRACTICE

13. Describe the regions of the pharynx.
14. List the major events of swallowing.
15. What is the function of the esophagus?

## 15.6 | Stomach

The **stomach** is a J-shaped, pouchlike organ that hangs inferior to the diaphragm in the upper left portion of the abdominal cavity and has a capacity of about 1 liter or more (figs. 15.1 and 15.11; see reference plates 4 and 5, pp. 35–36). Thick folds (rugae) of mucosal and submucosal layers mark the stomach's inner lining and disappear when the stomach wall is distended.

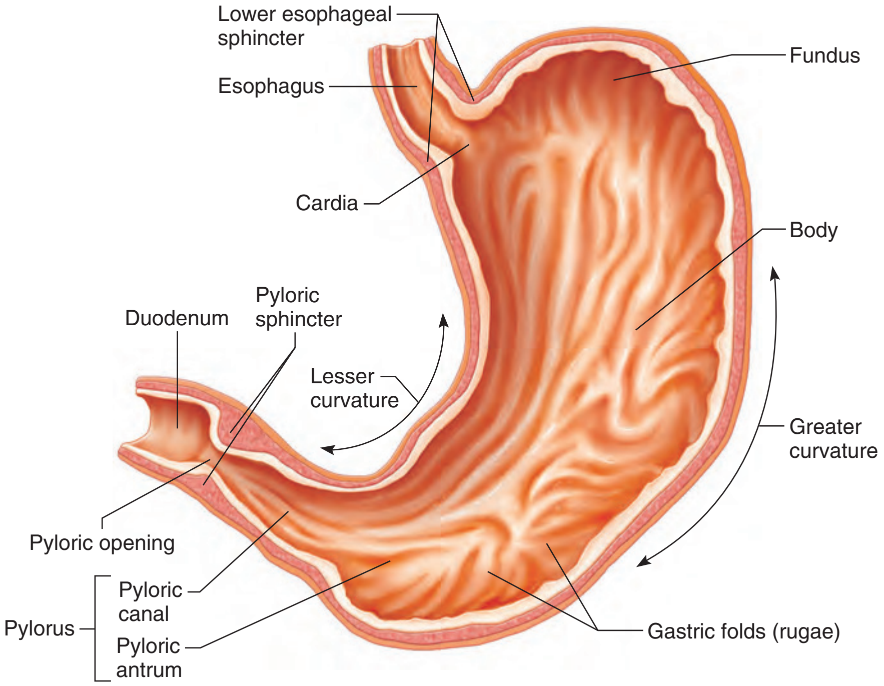


**FIGURE 15.11** APR Major regions of the stomach and its associated structures.

The stomach receives food from the esophagus, mixes the food with gastric juice, initiates protein digestion, carries on limited absorption, and moves food into the small intestine.

## Parts of the Stomach

The stomach is divided into the cardia, fundus, body, and pylorus (fig. 15.11). The *cardia* is a small area near the esophageal opening. The *fundus,* which balloons superior to the cardia, is a temporary storage area. The dilated *body region,* which is the main part of the stomach, lies between the fundus and pylorus. The **pyloric canal** is a narrowing of the *pylorus* as it approaches the small intestine.

At the end of the pyloric canal the muscular wall thickens, forming a powerful circular muscle, the **pyloric sphincter.** This muscle is a valve that controls gastric emptying.

## Gastric Secretions

The mucous membrane that forms the inner lining of the stomach is thick. Its surface is studded with many small openings called *gastric pits* located at the ends of tubular **gastric glands** (gas′trik glandz) (fig. 15.12).

Gastric glands generally contain three types of secretory cells. *Mucous cells*, in the necks of the glands near the openings of the gastric pits, secrete mucus. *Chief cells* and *parietal cells* are in the deeper parts of the glands. The chief cells secrete digestive enzymes, and the parietal cells release a solution containing hydrochloric acid. The products of the mucous cells, chief cells, and parietal cells together form **gastric juice** (gas′trik joos).

**Pepsin** (pep′sin) is by far the most important digestive enzyme in gastric juice. The chief cells secrete pepsin as the inactive enzyme precursor **pepsinogen** (pep-sin′o-jen). When pepsinogen contacts hydrochloric acid from the parietal cells, it breaks down rapidly, forming pepsin. Pepsin begins the digestion of nearly all types of dietary protein into polypeptides. This enzyme is most active in an acidic environment, which is provided by the hydrochloric acid in gastric juice.

The mucous cells of the gastric glands (*mucous neck cells*) and the mucous cells associated with the stomach's inner surface release a viscous, alkaline secretion that coats the inside of the stomach wall. This coating normally prevents the stomach from digesting itself.

Another component of gastric juice is **intrinsic factor** (in-trin′sik fak′tor), which the parietal cells secrete. Intrinsic factor helps the small intestine absorb vitamin $B_{12}$. Table 15.2 summarizes the components of gastric juice.

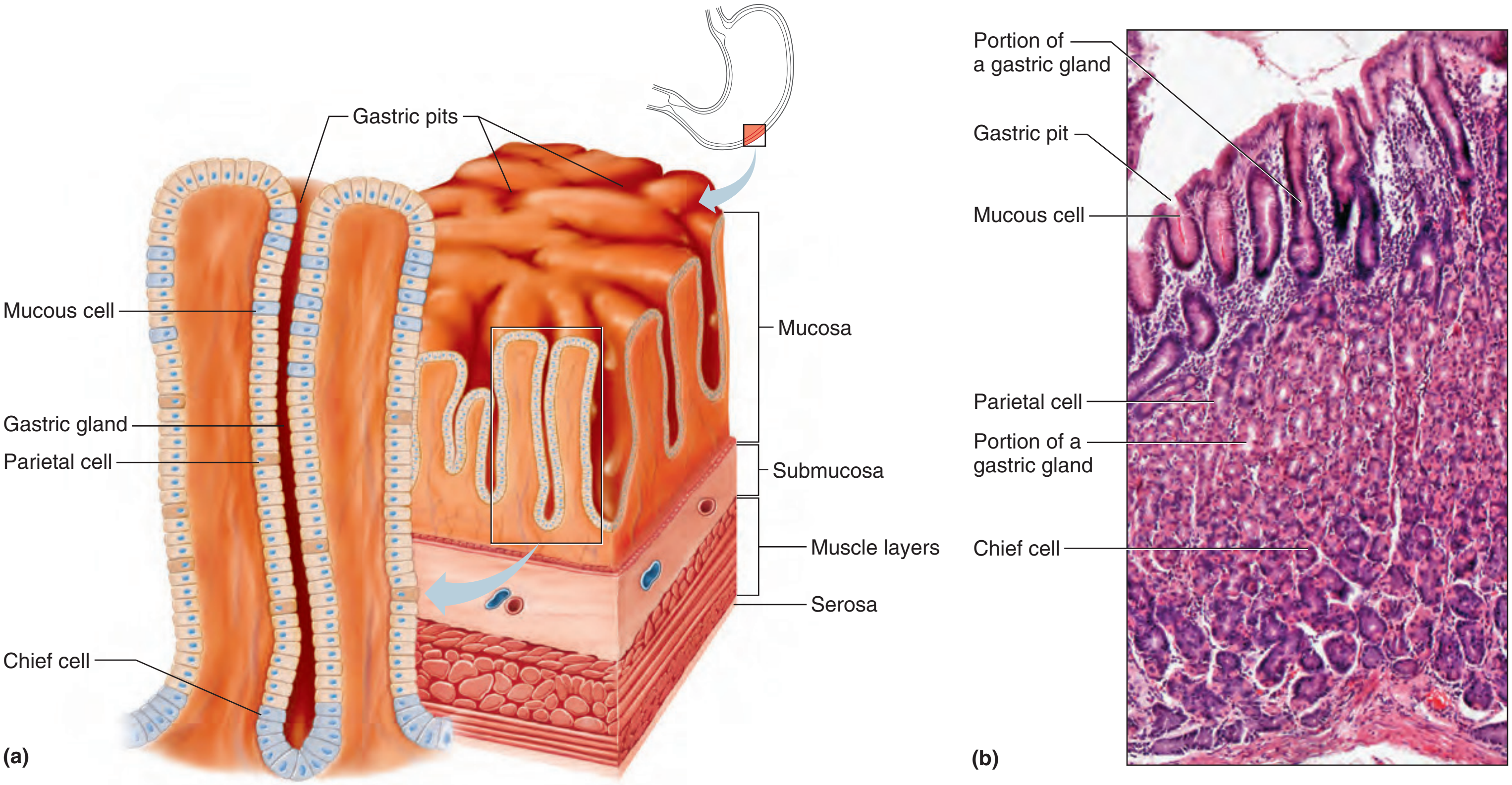


**FIGURE 15.12** APR Lining of the stomach. (**a**) Gastric glands include mucous cells, parietal cells, and chief cells. (**b**) A light micrograph of cells associated with the gastric glands (60×).

**TABLE 15.2** Major Components of Gastric Juice APR

| Component | Source | Function |
|---|---|---|
| Pepsinogen | Chief cells of the gastric glands | Inactive form of pepsin |
| Pepsin | Formed from pepsinogen in the presence of hydrochloric acid | A protein-splitting enzyme that digests nearly all types of dietary protein into polypeptides |
| Hydrochloric acid | Parietal cells of the gastric glands | Provides the acid environment needed for the production and action of pepsin |
| Mucus | Mucous cells | Provides a viscous, alkaline protective layer on the stomach's inner surface |
| Intrinsic factor | Parietal cells of the gastric glands | Aids in vitamin $B_{12}$ absorption in the intestine |

## PRACTICE

16. What are the secretions of the chief cells and parietal cells?
17. Which is the most important digestive enzyme in gastric juice?
18. Why doesn't the stomach digest itself?

**FACTS OF LIFE** The 40 million cells that line the stomach's interior can secrete 2 to 3 quarts (about 2 to 3 liters) of gastric juice per day.

## Regulation of Gastric Secretions

Gastric juice is produced continuously, but the rate varies considerably and is controlled both neurally and hormonally. When a person tastes, smells, or even sees appetizing food, or when food enters the stomach, parasympathetic impulses on the vagus nerves stimulate the release of the neurotransmitter acetylcholine (Ach). This Ach stimulates gastric glands to secrete abundant gastric juice, which is rich in hydrochloric acid and pepsinogen. These parasympathetic impulses also stimulate certain stomach cells to release the peptide hormone **gastrin** (gas′trin), which increases the secretory activity of gastric glands (fig. 15.13).

Gastrin stimulates cell growth in the mucosa of the stomach and intestines, except where gastrin is produced. This cell growth helps replace mucosal cells damaged by normal stomach function, disease, or medical treatments.

As food moves into the small intestine, acid triggers sympathetic impulses that inhibit gastric juice secretion. At the same time, proteins and fats in this region of the intestine cause the intestinal wall to release the peptide hormone **cholecystokinin** (ko″le-sis″to-ki′nin). This hormonal action decreases gastric motility as the small intestine fills with food.

An *ulcer* is an open sore in the skin or a mucous membrane resulting from localized tissue breakdown. Gastric ulcers form in the stomach, and duodenal ulcers form in the region of the small intestine nearest the stomach.

For many years, gastric and duodenal ulcers were attributed to stress and treated with medications to decrease stomach acid secretion. In 1982, two Australian researchers boldly suggested that stomach infection by the bacterium *Helicobacter pylori* causes gastric ulcers. When the medical community did not believe them, one of the researchers swallowed a solution of some bacteria, calling it "swamp water," to demonstrate the effect. The researchers soon developed stomach pain (gastritis). Today, a short course of antibiotics, often combined with drugs that decrease stomach acidity, can be used to treat many gastric ulcers.

## Gastric Absorption

Gastric enzymes begin breaking down proteins, but the stomach wall is not well adapted to absorbing digestive products. The stomach absorbs only small volumes of

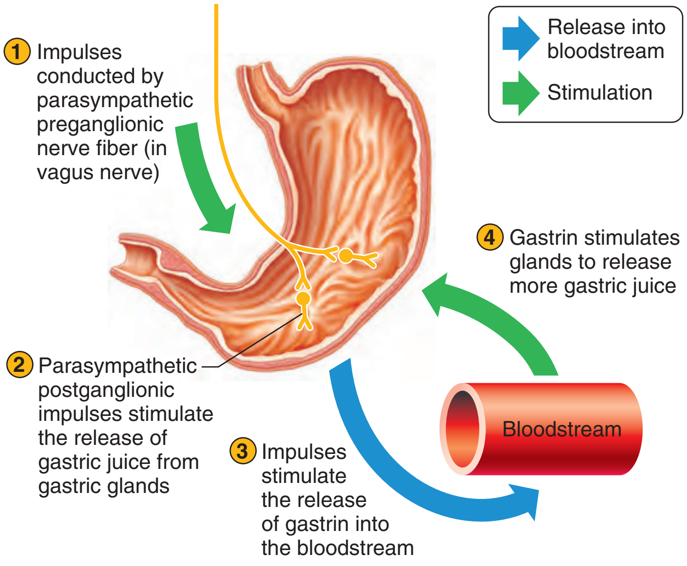

Release into bloodstream
Stimulation
① Impulses conducted by parasympathetic preganglionic nerve fiber (in vagus nerve)
④ Gastrin stimulates glands to release more gastric juice
② Parasympathetic postganglionic impulses stimulate the release of gastric juice from gastric glands
③ Impulses stimulate the release of gastrin into the bloodstream
Bloodstream

**FIGURE 15.13** APR The secretion of gastric juice is regulated in part by parasympathetic impulses that stimulate the release of gastric juice and gastrin.

water and certain salts as well as certain lipid-soluble drugs. Alcohol, which is not a nutrient, is absorbed both in the small intestine and in the stomach.

**PRACTICE**

19. What controls gastric juice secretion?
20. What is the function of cholecystokinin?
21. Which substances can the stomach absorb?

## Mixing and Emptying Actions

Following a meal, the mixing movements of the stomach wall aid in producing a semifluid paste of food particles and gastric juice called **chyme** (kīm). Peristaltic waves push the chyme toward the pylorus of the stomach and, as chyme accumulates near the pyloric sphincter, this muscle begins to relax. Stomach contractions push chyme a little at a time into the small intestine.

The rate at which the stomach empties depends on the fluidity of the chyme and the type of food present. Liquids usually pass through the stomach rapidly, but solids remain until they are well mixed with gastric juice. Fatty foods may remain in the stomach from three to six hours; foods high in proteins move through more quickly; carbohydrates usually pass through faster than either fats or proteins.

As chyme enters the duodenum (the proximal portion of the small intestine), accessory organs—the pancreas, liver, and gallbladder—add their secretions.

*Vomiting* results from a complex reflex that empties the stomach in the reverse of the normal direction. Irritation or distension in the stomach or intestines can trigger vomiting. Sensory impulses travel from the site of stimulation to the *vomiting center* in the medulla oblongata, and motor responses follow. These include taking a deep breath, raising the soft palate and thus closing the nasal cavity, closing the opening to the trachea (glottis), relaxing the circular muscle fibers at the base of the esophagus, contracting the diaphragm so it presses downward over the stomach, and contracting the abdominal wall muscles to increase pressure inside the abdominal cavity. As a result, the stomach is squeezed from all sides, forcing its contents upward and out via the open pathway through the esophagus, pharynx, and mouth.

**PRACTICE**

22. How is chyme produced?
23. What factors influence how quickly chyme leaves the stomach?

## 15.7 | Pancreas

The **pancreas** was discussed as an endocrine gland in chapter 11 (pp. 317–319). It also has an exocrine function—secretion of a digestive fluid called **pancreatic juice** (pan″kre-at′ik jo͞os).

### Structure of the Pancreas

The pancreas is closely associated with the small intestine. It extends horizontally across the posterior abdominal wall, with its head in the C-shaped curve of the duodenum and its tail against the spleen (figs. 15.1 and 15.14).

The cells that produce pancreatic juice, called *pancreatic acinar* (a′sĭ-nar) *cells,* make up the bulk of the pancreas. These cells cluster around tiny tubes into which they release their secretions. The smaller tubes unite to form larger ones, which in turn give rise to a *pancreatic duct* extending the length of the pancreas. The pancreatic duct usually connects with the duodenum at the same place where the bile duct from the liver and gallbladder joins the duodenum, although other connections may be present (fig. 15.14). A *hepatopancreatic sphincter* controls the movement of pancreatic juices into the duodenum.

### Pancreatic Juice

Pancreatic juice contains enzymes that digest carbohydrates, fats, nucleic acids, and proteins. The carbohydrate-digesting enzyme **pancreatic amylase** splits molecules of starch or glycogen into disaccharides. The fat-digesting enzyme **pancreatic lipase** breaks triglyceride molecules into fatty acids and glycerol. Pancreatic juice also contains two **nucleases,** which are enzymes that break down nucleic acid molecules into nucleotides.

The protein-splitting (proteolytic) enzymes are **trypsin, chymotrypsin,** and **carboxypeptidase** (kar-bok″se-pep′tĭ-dās). These enzymes split the bonds between particular combinations of amino acids in proteins. No single enzyme can split all possible amino acid combinations, so several enzymes are necessary to completely digest protein molecules.

The proteolytic enzymes are stored in tiny cellular structures called *zymogen granules* (zi-mo′jen gran′ūlz). These enzymes, like gastric pepsin, are secreted in inactive forms. After the inactive forms of the proteolytic enzymes reach the small intestine, other enzymes activate them. For example, pancreatic cells release inactive *trypsinogen,* which is activated to trypsin when it contacts the enzyme **enterokinase** (en″ter-o-ki′nās) secreted by the mucosa of the small intestine.

Painful *acute pancreatitis* results when pancreatic enzymes become active before they are secreted, and digest parts of the pancreas. Alcoholism, gallstones, certain infections, traumatic injuries, an inherited lipase deficiency, or the side effects of some drugs can cause pancreatitis.

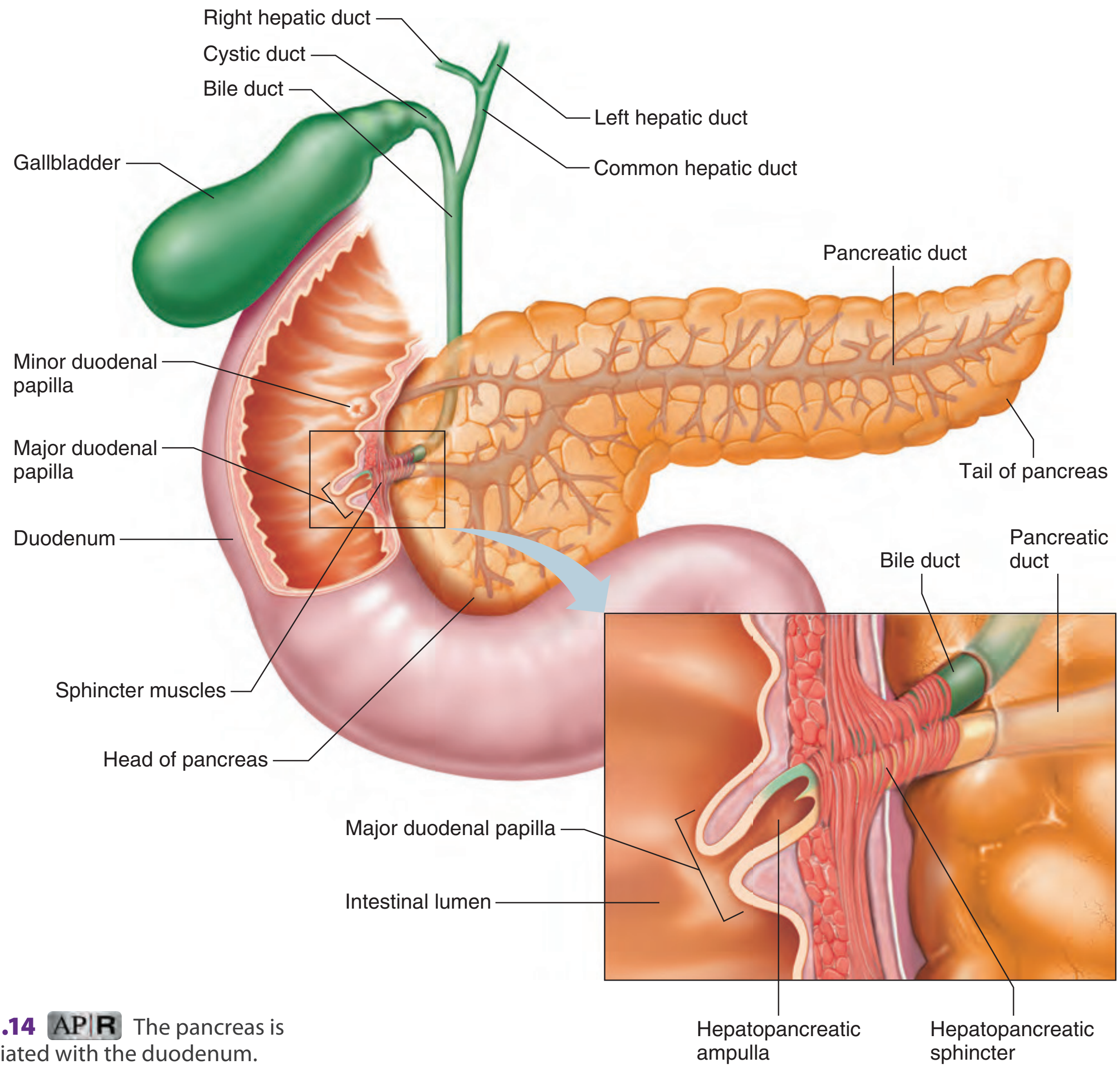

Right hepatic duct
Cystic duct
Bile duct
Gallbladder
Left hepatic duct
Common hepatic duct
Pancreatic duct
Minor duodenal papilla
Major duodenal papilla
Tail of pancreas
Duodenum
Bile duct
Pancreatic duct
Sphincter muscles
Head of pancreas
Major duodenal papilla
Intestinal lumen
Hepatopancreatic ampulla
Hepatopancreatic sphincter

**FIGURE 15.14** APR The pancreas is closely associated with the duodenum.

## Regulation of Pancreatic Secretion

The nervous and endocrine systems regulate release of pancreatic juice, as they do gastric and small intestinal secretions. For example, when parasympathetic impulses stimulate gastric juice secretion, other parasympathetic impulses stimulate the pancreas to release digestive enzymes. Also, as acidic chyme enters the duodenum, the duodenal mucous membrane releases the peptide hormone **secretin** (se-kre′tin) into the bloodstream (fig. 15.15). This hormone stimulates secretion of pancreatic juice that has a high concentration of bicarbonate ions. These ions neutralize the acid in chyme and provide a favorable environment for digestive enzymes in the intestine.

Proteins and fats in chyme in the duodenum also stimulate the intestinal wall to release *cholecystokinin*. Like secretin, cholecystokinin travels via the bloodstream to the pancreas. Pancreatic juice secreted in response to cholecystokinin has a high concentration of digestive enzymes.

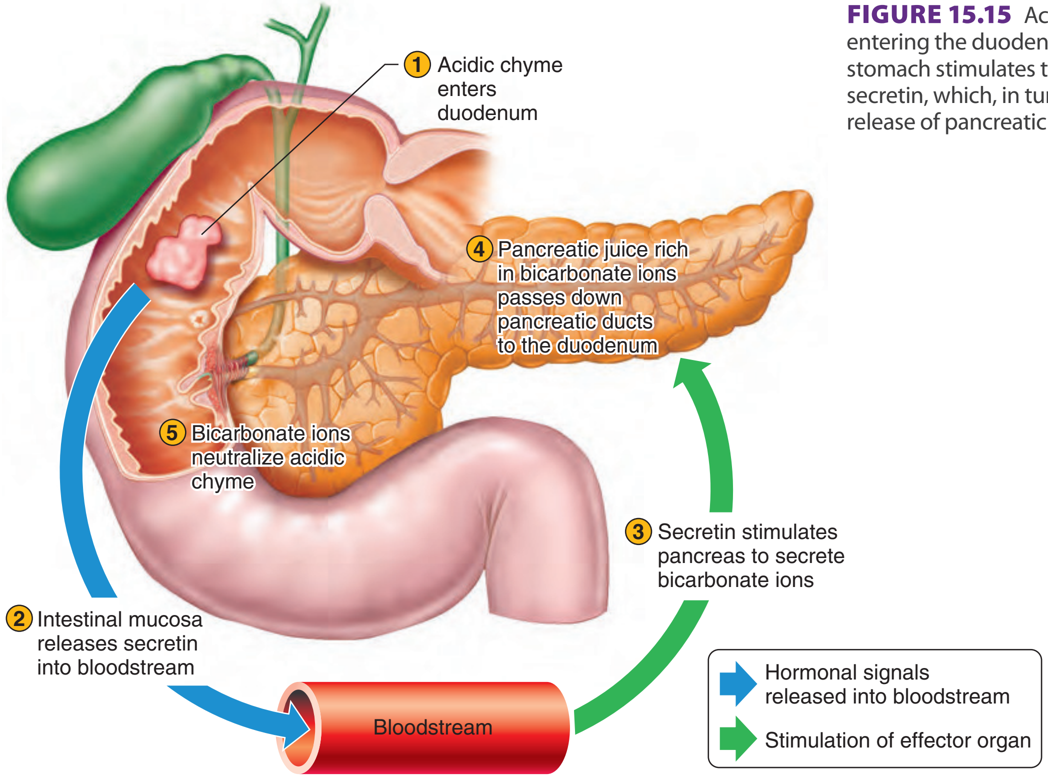
### PRACTICE

24. List the enzymes in pancreatic juice.
25. What are the functions of the enzymes in pancreatic juice?
26. What regulates secretion of pancreatic juice?

## 15.8 | Liver

The **liver** is in the upper right quadrant of the abdominal cavity, just inferior to the diaphragm. It is partially surrounded by the ribs, and extends from the level of the fifth intercostal space to the lower margin of the ribs. The reddish-brown liver is well supplied with blood vessels (see fig. 15.1 and reference plate 4, p. 35).

**FACTS OF LIFE** The adult liver is the heaviest internal organ in the body. On average it weighs about 3 pounds.



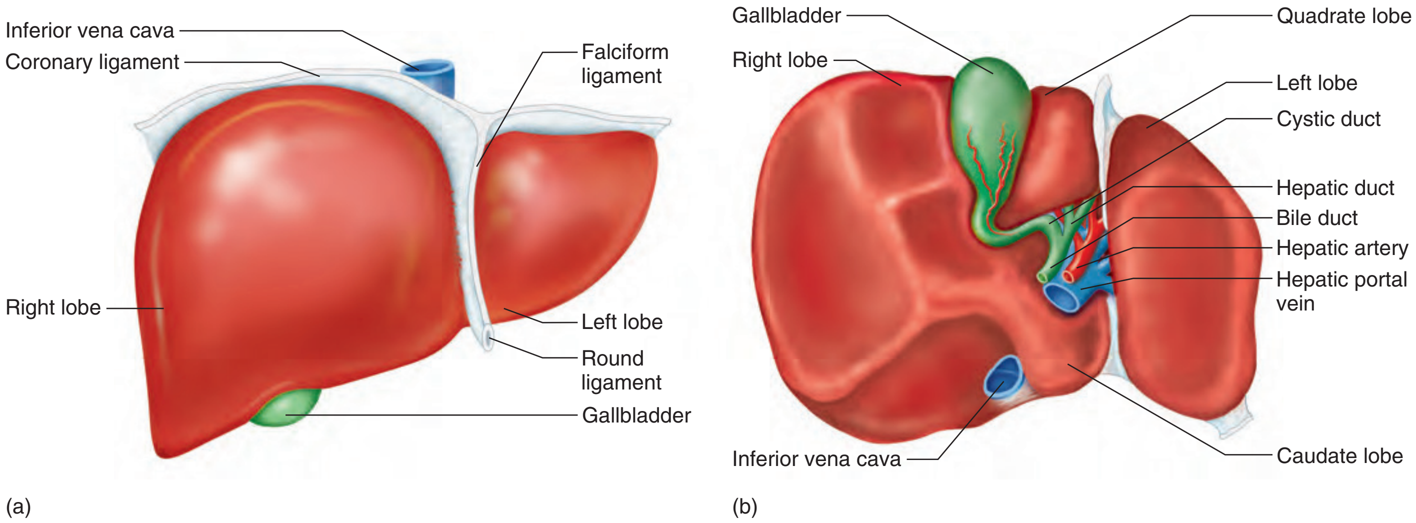
① Acidic chyme enters duodenum
② Intestinal mucosa releases secretin into bloodstream
Bloodstream
③ Secretin stimulates pancreas to secrete bicarbonate ions
④ Pancreatic juice rich in bicarbonate ions passes down pancreatic ducts to the duodenum
⑤ Bicarbonate ions neutralize acidic chyme
Hormonal signals released into bloodstream
Stimulation of effector organ

**FIGURE 15.15** Acidic chyme entering the duodenum from the stomach stimulates the release of secretin, which, in turn, stimulates the release of pancreatic juice.

## Liver Structure

A fibrous capsule encloses the liver, and ligaments divide the organ into a large *right lobe* and a smaller *left lobe* (fig. 15.16). The liver also has two minor lobes, the *quadrate lobe* and the *caudate lobe*. Each lobe is separated into many tiny **hepatic lobules** (hĕ-pat′ik lob′ulz), the liver's functional units (fig. 15.17). A lobule consists of many hepatic cells radiating outward from a *central vein*. Vascular channels called **hepatic sinusoids** separate platelike groups of these cells from each other. Blood from the digestive tract, carried in the *hepatic portal vein* (see chapter 13, pp. 379–380), brings newly absorbed nutrients into the sinusoids and nourishes the hepatic cells (fig. 15.18).

Large phagocytic macrophages called *Kupffer cells* (koop′fer selz) are fixed to the inner linings of the hepatic sinusoids. They remove bacteria or other foreign particles that enter the blood in the portal vein through the intestinal wall. Blood passes from these sinusoids into the central veins of the hepatic lobules and exits the liver via the hepatic vein.



Inferior vena cava
Coronary ligament
Falciform ligament
Right lobe
Left lobe
Round ligament
Gallbladder
(a)
Gallbladder
Right lobe
Quadrate lobe
Left lobe
Cystic duct
Hepatic duct
Bile duct
Hepatic artery
Hepatic portal vein
Inferior vena cava
Caudate lobe
(b)

**FIGURE 15.16** APR Lobes of the liver, viewed (**a**) anteriorly and (**b**) inferiorly.

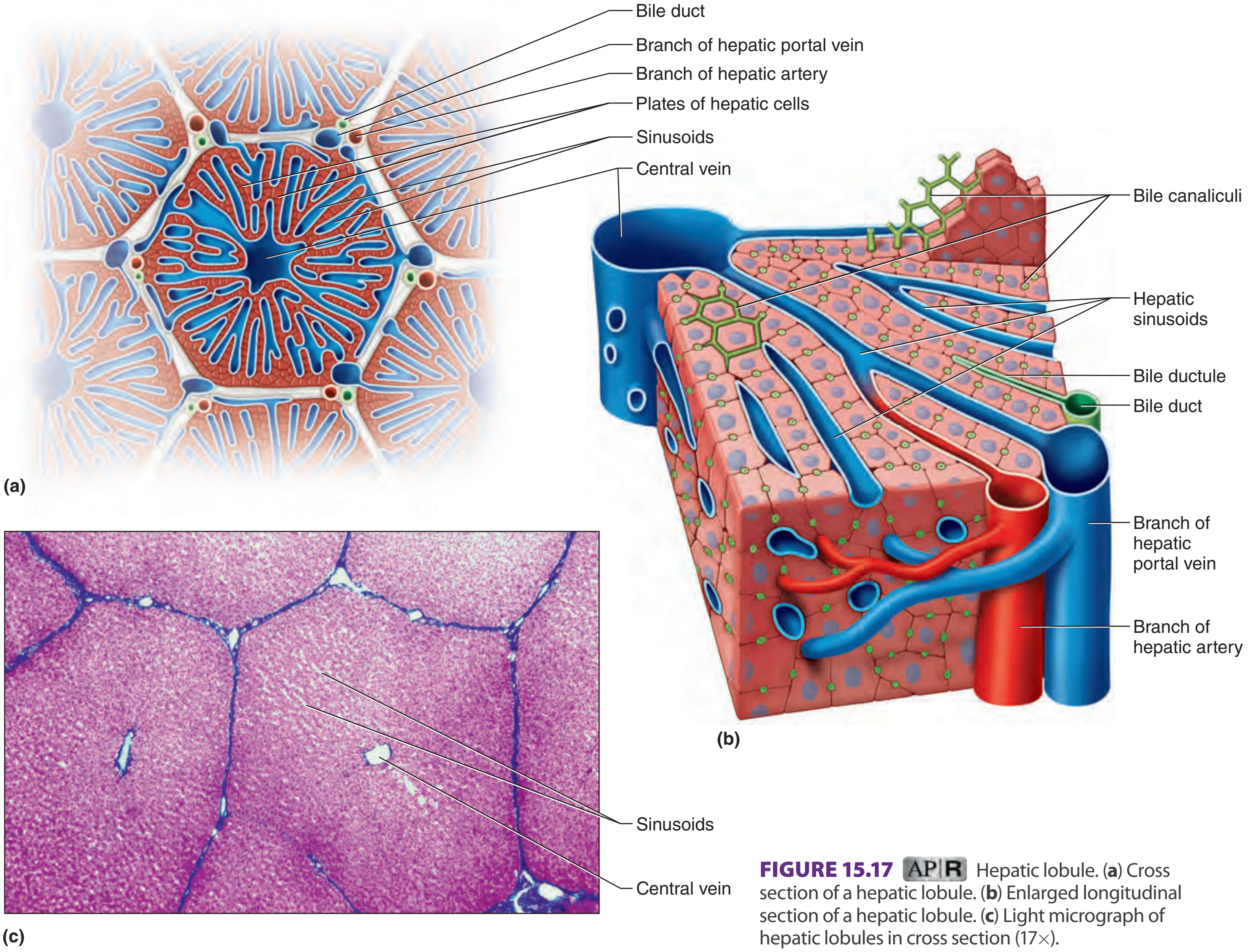

Bile duct
Branch of hepatic portal vein
Branch of hepatic artery
Plates of hepatic cells
Sinusoids
Central vein
(a)
Bile canaliculi
Hepatic sinusoids
Bile ductule
Bile duct
Branch of hepatic portal vein
Branch of hepatic artery
(b)
Sinusoids
Central vein
(c)

**FIGURE 15.17** APR Hepatic lobule. (**a**) Cross section of a hepatic lobule. (**b**) Enlarged longitudinal section of a hepatic lobule. (**c**) Light micrograph of hepatic lobules in cross section (17×).

Within the hepatic lobules are many fine *bile canaliculi,* which carry secretions from hepatic cells to *bile ductules* (fig. 15.18). The ductules of neighboring lobules converge to ultimately form the **hepatic ducts.** These ducts merge, in turn, to form the **common hepatic duct.**

## Liver Functions

The liver carries on many important metabolic activities. Recall from chapter 11 (pp. 317–319) that the liver plays a key role in carbohydrate metabolism by helping maintain concentration of blood glucose within the normal range. Liver cells responding to hormones such as insulin and glucagon lower the blood glucose level by polymerizing glucose to glycogen, and raise the blood glucose level by breaking down glycogen to glucose or by converting noncarbohydrates into glucose.

The liver's effects on lipid metabolism include oxidizing fatty acids at an especially high rate; synthesizing lipoproteins, phospholipids, and cholesterol; and converting excess portions of carbohydrate molecules into fat molecules. The blood transports fats synthesized in the liver to adipose tissue for storage.

The most vital liver functions concern protein metabolism. They include deaminating amino acids; forming urea (see p. 441); synthesizing plasma proteins, such as clotting factors (see chapter 12, p. 338); and converting certain amino acids into other amino acids.

The liver also stores many substances, including glycogen, iron, and vitamins A, D, and $B_{12}$. In addition, macrophages in the liver help destroy damaged red blood cells (see chapter 12, p. 331) and phagocytize foreign antigens. The liver also removes toxic substances such as alcohol and certain other drugs from blood (detoxification) and secretes bile.

Many of these liver functions are not directly related to the digestive system and are, as indicated above, discussed in other chapters. Bile secretion, however, is important to digestion and is explained next in this chapter. Table 15.3 summarizes the major functions of the liver. Clinical Application 15.2 discusses viral infections of the liver.

The liver is unlike most organs in that it can regenerate. Up to 75% of a liver can be destroyed and the organ can still regenerate and recover. For this reason, people can donate parts of their livers to people in liver failure, if the tissues of donor and recipient are compatible.

**PRACTICE**

27. Locate the liver.
28. Describe a hepatic lobule.
29. Review liver functions.

## Composition of Bile

**Bile** (bīl) is a yellowish-green liquid continuously secreted from hepatic cells. In addition to water, bile contains *bile salts, bile pigments* (bilirubin and biliverdin), *cholesterol,* and *electrolytes.* Of these, bile salts are the most abundant and are the only bile components that have a digestive function. Bile pigments are breakdown products of hemoglobin from red blood cells and are normally secreted in the bile (see chapter 12, p. 333).

**TABLE 15.3 Major Functions of the Liver**

| General Function | Specific Function |
|---|---|
| Carbohydrate metabolism | Polymerizes glucose to glycogen; breaks down glycogen to glucose; converts noncarbohydrates to glucose |
| Lipid metabolism | Oxidizes fatty acids; synthesizes lipoproteins, phospholipids, and cholesterol; converts excess portions of carbohydrate molecules into fats |
| Protein metabolism | Deaminates amino acids; forms urea; synthesizes plasma proteins; converts certain amino acids into other amino acids |
| Storage | Stores glycogen, iron, and vitamins A, D, and $B_{12}$ |
| Blood filtering | Removes damaged red blood cells and foreign substances by phagocytosis |
| Detoxification | Removes toxins from blood |
| Secretion | Produces and secretes bile |

Jaundice, a yellowing of the skin and mucous membranes due to accumulation of bile pigment, has several causes. In *obstructive jaundice* bile ducts are blocked, perhaps by gallstones or tumors. In *hepatocellular jaundice* the liver is diseased, as in cirrhosis or hepatitis. In *hemolytic jaundice* red blood cells are destroyed too rapidly, as happens with an incompatible blood transfusion or a blood infection.

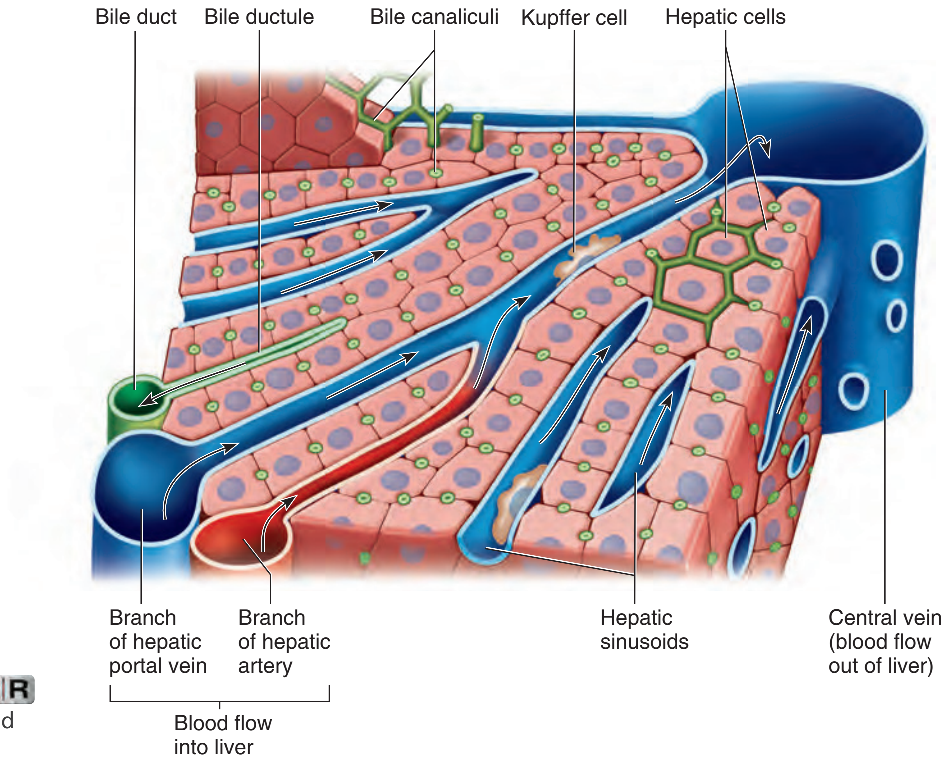


**FIGURE 15.18** APR The paths of blood and bile within a hepatic lobule.

### CLINICAL APPLICATION 15.2

### Hepatitis

*Hepatitis* is an inflammation of the liver. About half a million people develop hepatitis in the United States each year, and 6,000 die of the disease. Hepatitis has several causes, but the various types have similar symptoms.

Acute hepatitis may at first resemble the flu, producing mild headache, low fever, fatigue, lack of appetite, nausea and vomiting, and sometimes stiff joints. By the end of the first week, more distinctive symptoms arise: a rash, pain in the upper right quadrant of the abdomen, dark and foamy urine, and pale feces. The skin and sclera of the eyes turn yellow due to accumulating bile pigments (jaundice). Great fatigue may continue for two or three weeks, and then gradually the person begins to feel better. This is hepatitis in its most common, least dangerous acute guise. In a rare acute form called *fulminant hepatitis,* symptoms are sudden and severe, along with altered behavior and personality. Medical attention is necessary to prevent kidney or liver failure or coma.

Chronic hepatitis persists for more than six months. As many as 300 million people worldwide are hepatitis carriers. They do not have symptoms but can infect others. Five percent of carriers eventually develop liver cancer.

Only rarely does hepatitis result from alcoholism, autoimmunity, or the use of certain drugs. Usually, one of several types of viruses cause hepatitis. Viral types are distinguished by the route of infection, surface features, and whether the viral genetic material is DNA or RNA. Hepatitis B virus has DNA; the others have RNA. The viral types are classified as follows:

*Hepatitis A* spreads by contact with food or objects contaminated with virus-containing feces, including diapers. The course of hepatitis A is short and mild.

*Hepatitis B* spreads by contact with virus-containing body fluids, such as blood, saliva, or semen. It may be transmitted by blood transfusions, hypodermic needles, or sexual activity.

*Hepatitis C* accounts for about half of all known cases of hepatitis. This virus is primarily transmitted in blood—by sharing razors or needles, from pregnant woman to fetus, or through blood transfusions or use of blood products. As many as 60% of individuals infected with the hepatitis C virus suffer chronic symptoms.

*Hepatitis D* infection occurs in people already infected with the hepatitis B virus. It is blood-borne and associated with blood transfusions and intravenous drug use. About 20% of individuals infected with this virus die from the infection.

*Hepatitis E* virus is usually transmitted in water contaminated with feces. It most often affects visitors to developing nations.

*Hepatitis G* infection is rare but accounts for a significant percentage of cases of fulminant hepatitis. In people with healthy immune systems, the virus produces symptoms so mild that they may not be noticed.

Antibiotic drugs, which are effective against bacteria, are not helpful against viral hepatitis. Usually, the person must just wait out the symptoms. Many cases of hepatitis C resolve on their own or respond to a 6 to 12 month course of a form of interferon or either of two new drugs.

## Gallbladder

The **gallbladder** (gawl′blad-er) is a pear-shaped sac in a depression on the liver's inferior surface. It connects to the **cystic duct** (sis′tik dukt), which in turn joins the common hepatic duct (figs. 15.1 and 15.19). The gallbladder is lined with epithelial cells and has a strong, muscular layer in its wall. The gallbladder stores bile between meals, reabsorbs water to concentrate bile, and contracts to release bile into the small intestine.

The common hepatic and cystic ducts join to form the *bile duct* (common bile duct). It leads to the duodenum where the *hepatopancreatic sphincter* guards its exit (figs. 15.14 and 15.19). This sphincter normally remains contracted, so as bile collects in the bile duct it backs up into the cystic duct. When this happens, bile flows into the gallbladder, where it is stored.

Cholesterol in bile may precipitate and form crystals called *gallstones* under certain conditions (fig. 15.20). Gallstones in the bile duct may block bile flow into the small intestine and cause considerable pain. A surgical procedure called a *cholecystectomy* removes the gallbladder when gallstones are obstructive. The surgery can often be done with a laparoscope (small, lit probe) on an outpatient basis.

## Regulation of Bile Release

Normally bile does not enter the duodenum until *cholecystokinin* stimulates the gallbladder to contract. The intestinal mucosa releases this hormone in response to proteins and fats in the small intestine. (Recall its action to stimulate pancreatic enzyme secretion, p. 424.) The hepatopancreatic sphincter usually remains contracted until a peristaltic wave in the duodenal wall approaches it. Then the sphincter relaxes, and bile is squirted into

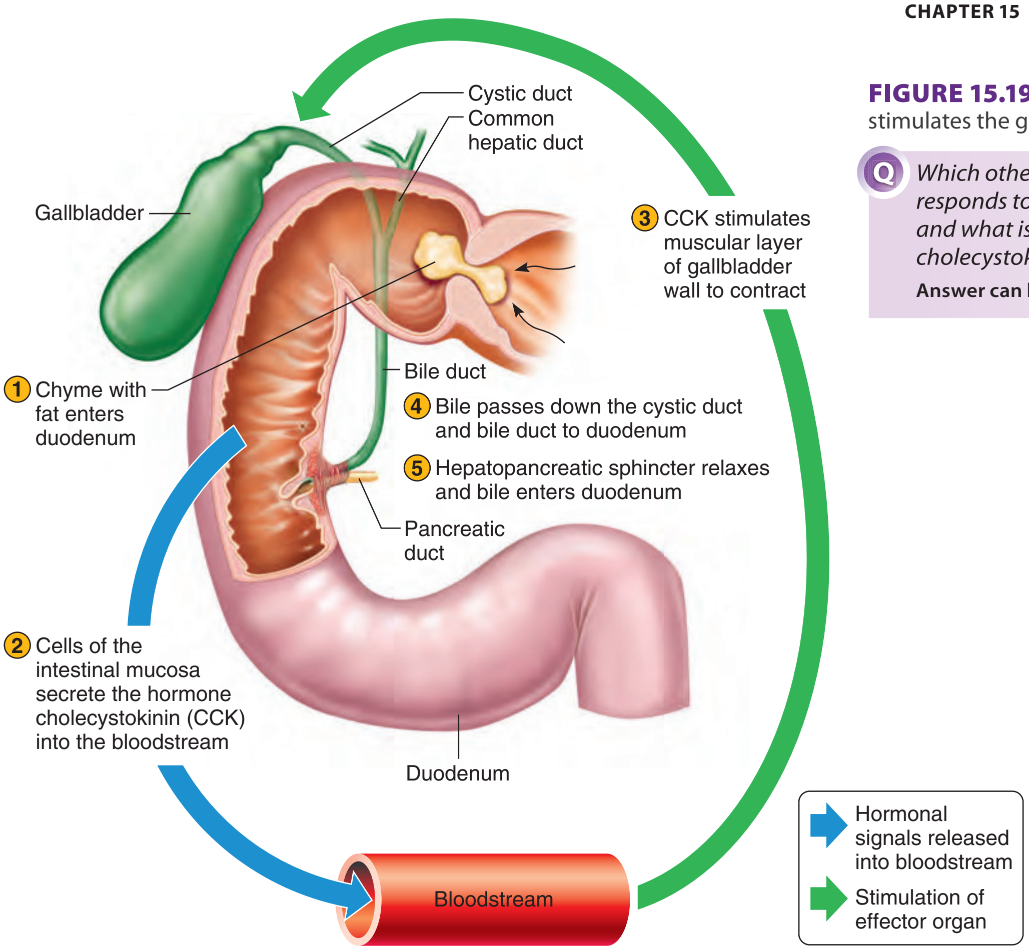

Cystic duct
Common hepatic duct
Gallbladder
③ CCK stimulates muscular layer of gallbladder wall to contract
① Chyme with fat enters duodenum
Bile duct
④ Bile passes down the cystic duct and bile duct to duodenum
⑤ Hepatopancreatic sphincter relaxes and bile enters duodenum
Pancreatic duct
② Cells of the intestinal mucosa secrete the hormone cholecystokinin (CCK) into the bloodstream
Duodenum
Bloodstream
Hormonal signals released into bloodstream
Stimulation of effector organ

**FIGURE 15.19** Fatty chyme entering the duodenum stimulates the gallbladder to release bile.

**Q** *Which other organ, besides the gallbladder, responds to cholecystokinin stimulation, and what is the response of that organ to cholecystokinin stimulation?*

**Answer can be found in Appendix F on page 582.**

**TABLE 15.4 Hormones of the Digestive Tract**

| Hormone | Source | Function |
|---|---|---|
| Gastrin | Gastric cells, in response to food | Increases secretory activity of gastric glands |
| Cholecystokinin | Intestinal wall cells, in response to proteins and fats in the small intestine | Decreases secretory activity of gastric glands and inhibits gastric motility; stimulates pancreas to secrete fluid with a high digestive enzyme concentration; stimulates gallbladder to contract and release bile |
| Secretin | Cells in the duodenal wall, in response to acidic chyme entering the small intestine | Stimulates pancreas to secrete fluid with a high bicarbonate ion concentration |

the duodenum (see fig. 15.19). Table 15.4 summarizes the hormones that help control digestion.

## Functions of Bile Salts

Bile salts aid digestive enzymes. Bile salts affect *fat globules* (clumped molecules of fats) much like a soap or detergent would affect them. That is, bile salts break fat globules into smaller droplets that are more soluble in water, an action called **emulsification** (e-mul″sĭ-fĭ-ka′shun), that greatly increases the total surface area of the fatty substance. The resulting fat droplets disperse in water. Fat-splitting enzymes (lipases) can then digest fat molecules more effectively.

Bile salts also enhance absorption of fatty acids, cholesterol, and the fat-soluble vitamins A, D, E, and K.

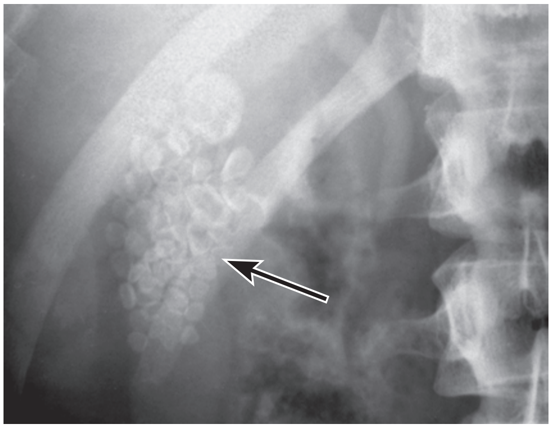


**FIGURE 15.20** Falsely colored radiograph of a gallbladder that contains gallstones (arrow).

Lack of bile salts results in poor lipid absorption and vitamin deficiencies.

**PRACTICE**

30. Explain how bile forms.
31. Describe the function of the gallbladder.
32. How is secretion of bile regulated?
33. How do bile salts function in digestion?

## 15.9 | Small Intestine

The **small intestine** is a tubular organ that extends from the pyloric sphincter to the beginning of the large intestine. With its many loops and coils, it fills much of the abdominal cavity (see fig. 15.1 and reference plates 4 and 5, pp. 35–36).

The small intestine receives chyme from the stomach and secretions from the pancreas and liver. It completes digestion of the nutrients in chyme, absorbs the products of digestion, and transports the residues to the large intestine.

### Parts of the Small Intestine

The small intestine consists of three parts: the duodenum, the jejunum, and the ileum (figs. 15.21 and 15.22). The **duodenum** (du″o-de′num), about 25 centimeters long and 5 centimeters in diameter, lies posterior to the parietal peritoneum and is the most fixed portion of the small intestine. It follows a C-shaped path as it passes anterior to the right kidney and the upper three lumbar vertebrae.

The remainder of the small intestine is mobile and lies free in the peritoneal cavity. The proximal two-fifths of this portion of the small intestine is the **jejunum** (jĕ-joo′num), and the remainder is the **ileum** (il′e-um). The jejunum and ileum are not distinctly separate parts; however, the diameter of the jejunum is typically greater than that of the ileum, and its wall is thicker, more vascular, and more active.

A double-layered fold of peritoneal membrane called **mesentery** (mes′en-ter″e) suspends these parts from the posterior abdominal wall (figs. 15.21, 15.23 and reference plate 5, p. 36). The mesentery supports the blood vessels, nerves, and lymphatic vessels that supply the intestinal wall.

A filmy, double fold of peritoneal membrane called the *greater omentum* drapes like an apron from the stomach over the transverse colon and the folds of the small intestine (fig. 15.23 and reference plate 3, p. 34). If the wall of the alimentary canal becomes infected, cells from the omentum may adhere to the inflamed region, helping to wall off the area. This action prevents spread of the infection to the peritoneal cavity.

### Structure of the Small Intestinal Wall

The inner surface of the small intestine throughout its length appears velvety due to many tiny projections of mucous membrane called **intestinal villi** (in-tes′tĭ-nal vil′i) (figs. 15.24 and 15.25; see fig. 15.3). These structures are most numerous in the duodenum and the proximal jejunum. They project into the lumen of the alimentary canal, contacting the intestinal contents. Villi greatly increase the surface area of the intestinal lining, aiding the absorption of digestive products.

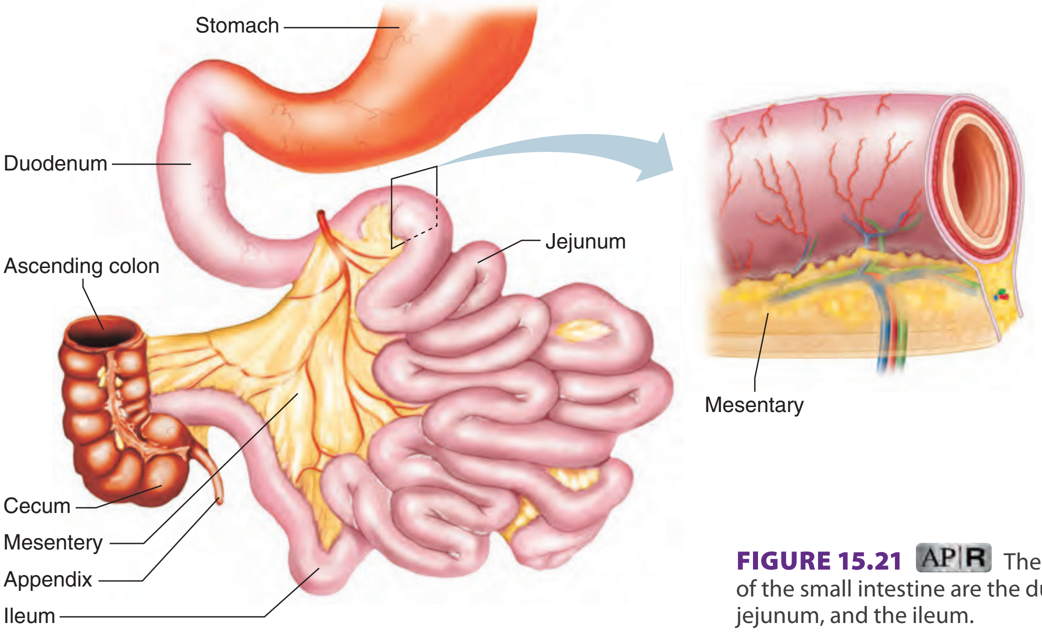


**FIGURE 15.21** APR The three parts of the small intestine are the duodenum, the jejunum, and the ileum.

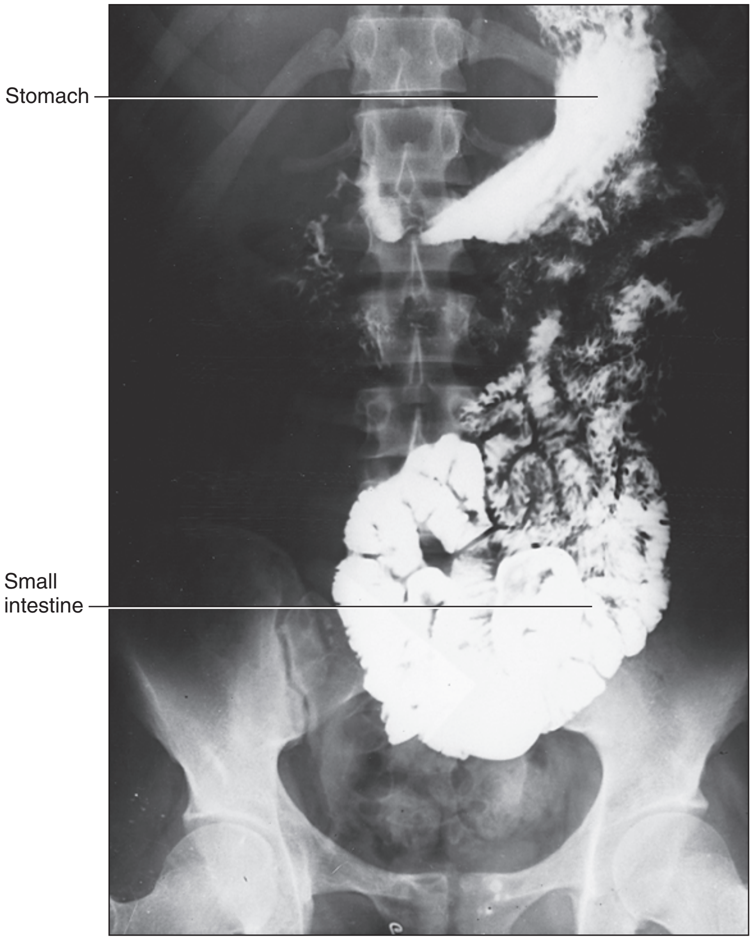

Stomach
Small intestine

**FIGURE 15.22** Radiograph showing a normal small intestine containing a radiopaque substance that the patient ingested.

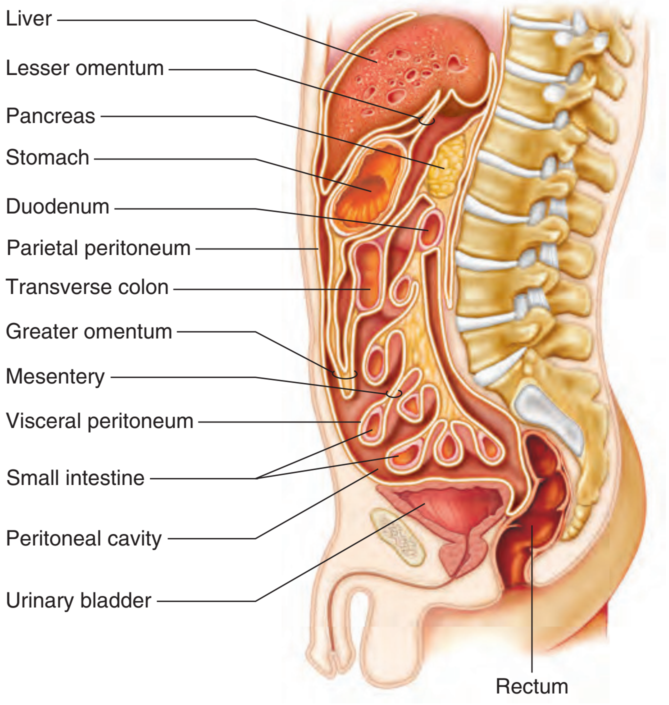

Liver
Lesser omentum
Pancreas
Stomach
Duodenum
Parietal peritoneum
Transverse colon
Greater omentum
Mesentery
Visceral peritoneum
Small intestine
Peritoneal cavity
Urinary bladder
Rectum

**FIGURE 15.23** Mesentery formed by folds of the peritoneal membrane suspends portions of the small intestine from the posterior abdominal wall.

Each villus consists of a layer of simple columnar epithelium and a core of connective tissue containing blood capillaries, a lymphatic capillary called a **lacteal,** and nerve fibers. Blood capillaries and lacteals carry away absorbed nutrients, and nerve fibers conduct impulses to stimulate or inhibit villus activities. Between the bases of adjacent villi are tubular **intestinal glands** that extend downward into the mucous membrane (figs. 15.24 and 15.25; see fig. 15.3).

The epithelial cells that form the lining of the small intestine are continually replaced. New cells form in the intestinal glands by mitosis and migrate outward onto the villus surface. When the migrating cells reach the tip of the villus, they are shed. As a result, nearly one-quarter of the bulk of feces consists of dead epithelial cells from the small intestine. This *cellular turnover* renews the small intestine's epithelial lining every three to six days.

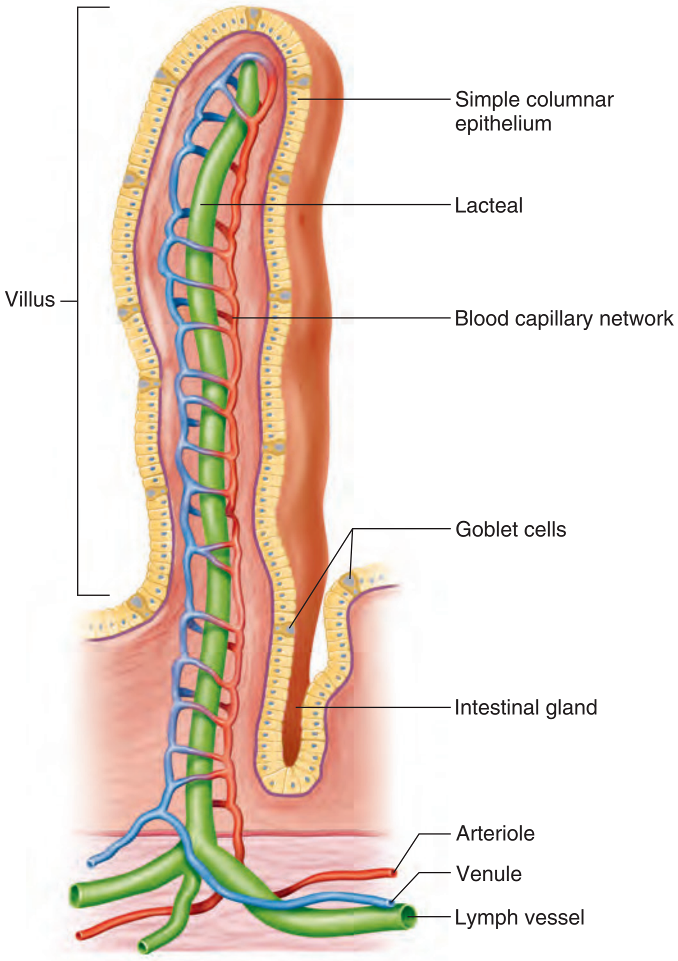

Villus
Simple columnar epithelium
Lacteal
Blood capillary network
Goblet cells
Intestinal gland
Arteriole
Venule
Lymph vessel

**FIGURE 15.24** Structure of a single intestinal villus. The elongated shapes of intestinal villi dramatically increase the absorptive surface area of the small intestine.

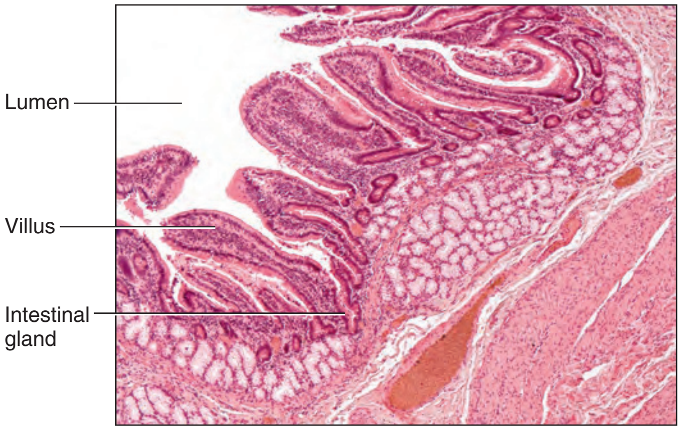


**FIGURE 15.25** APR Light micrograph of intestinal villi from the wall of the duodenum (50×).

## Secretions of the Small Intestine

Mucus-secreting goblet cells are abundant throughout the mucosa of the small intestine. In addition, many specialized *mucus-secreting glands* in the submucosa in the proximal portion of the duodenum secrete a thick, alkaline mucus in response to certain stimuli.

The intestinal glands at the bases of the villi secrete large volumes of a watery fluid, which brings digestive products to the villi. The fluid has a nearly neutral pH (6.5–7.5), and it lacks digestive enzymes. However, the epithelial cells of the intestinal mucosa have digestive enzymes embedded in the membranes of their microvilli on their luminal surfaces. These enzymes break down food molecules just before absorption takes place. The enzymes include **peptidases,** which split peptides into their constituent amino acids; **sucrase, maltase,** and **lactase,** which split the disaccharides sucrose, maltose, and lactose into the monosaccharides glucose, fructose, and galactose; and **intestinal lipase,** which splits fats into fatty acids and glycerol. Table 15.5 summarizes the sources and actions of the major digestive enzymes.

## Regulation of Small Intestine Secretions

Goblet cells and intestinal glands secrete their products when chyme provides both mechanical and chemical stimulation. Distension of the intestinal wall activates the nerve plexuses within the wall and stimulates parasympathetic reflexes that also trigger release of small intestine secretions.

**PRACTICE**

34. Describe the parts of the small intestine.
35. What is the function of an intestinal villus?
36. What is the function of the intestinal glands?
37. List the intestinal digestive enzymes.

Adults who have *lactose intolerance* do not produce sufficient lactase to adequately digest lactose, or milk sugar. Undigested lactose increases the osmotic pressure of the intestinal contents and draws water into the intestines. At the same time, intestinal bacteria metabolize undigested sugar, producing organic acids and gases. The overall result is bloating, intestinal cramps, and diarrhea.

Genetic evidence suggests that lactose intolerance may be the "normal" condition, with ability to digest lactose the result of a mutation that occurred recently in our evolutionary past and became advantageous when the advent of agriculture brought dairy foods to human populations. The trait of ability to digest lactose has increased with the increased use of dairy foods at least three times in history, in different populations.

## Absorption in the Small Intestine

Villi greatly increase the surface area of the intestinal mucosa, making the small intestine the most important absorbing organ of the alimentary canal. So effective

**TABLE 15.5 Summary of the Major Digestive Enzymes**

| Enzyme | Source | Digestive Action |
|---|---|---|
| Salivary amylase | Salivary glands | Begins carbohydrate digestion by breaking down starch and glycogen to disaccharides |
| Pepsin | Gastric chief cells | Begins protein digestion |
| Pancreatic amylase | Pancreas | Breaks down starch and glycogen into disaccharides |
| Pancreatic lipase | Pancreas | Breaks down fats into fatty acids and glycerol |
| Proteolytic enzymes<br>(a) Trypsin<br>(b) Chymotrypsin<br>(c) Carboxypeptidase | Pancreas | Breaks down proteins or partially digested proteins into peptides |
| Nucleases | Pancreas | Breaks down nucleic acids into nucleotides |
| Peptidase | Intestinal mucosal cells | Breaks down peptides into amino acids |
| Sucrase, maltase, lactase | Intestinal mucosal cells | Breaks down disaccharides into monosaccharides |
| Intestinal lipase | Intestinal mucosal cells | Breaks down fats into fatty acids and glycerol |
| Enterokinase | Intestinal mucosal cells | Converts trypsinogen into trypsin |

is the small intestine in absorbing digestive products, water, and electrolytes that very little absorbable material reaches its distal end.

Carbohydrate digestion begins in the mouth with the activity of salivary amylase, and is completed in the small intestine by enzymes from the intestinal mucosa and pancreas. Villi absorb the resulting monosaccharides, which enter blood capillaries. Simple sugars are absorbed by facilitated diffusion or active transport (see chapter 3, pp. 73 and 75–76)

Protein digestion begins in the stomach as a result of pepsin activity, and is completed in the small intestine by enzymes from the intestinal mucosa and the pancreas. During this process, large protein molecules are broken down into amino acids, which are then actively transported into the villi and carried away by the blood.

Fat molecules are digested almost entirely by enzymes from the pancreas and intestinal mucosa. The resulting fatty acids and glycerol molecules diffuse into villi epithelial cells (fig. 15.26 *(1)*). The endoplasmic reticula of the cells use the fatty acids to resynthesize fat molecules similar to those previously digested (fig. 15.26 *(2)*). These fats are encased in protein to form *chylomicrons* (fig. 15.26 *(3)*), which make their way to the lacteals of the villi (fig. 15.26 *(4)*). Lymph in the lacteals and other lymphatic vessels carries chylomicrons to the bloodstream, as discussed in chapter 14 on page 387 (fig. 15.26 *(5)*). Some fatty acids with very short carbon chains may be absorbed directly into the blood capillary of a villus without being changed back into fat.

Chylomicrons transport dietary fats to muscle and adipose cells. Similarly, VLDL (very low-density lipoprotein with a high concentration of triglycerides) molecules, produced in the liver, transport triglycerides synthesized from excess dietary carbohydrates. As VLDL molecules reach adipose cells, an enzyme, *lipoprotein lipase,* catalyzes reactions that unload their triglycerides, converting the VLDL to LDL (low-density lipoproteins). Because most of the triglycerides have been removed, LDL molecules have a higher cholesterol content than do the original VLDL molecules. Cells in the peripheral tissues remove LDL from plasma by receptor-mediated endocytosis, thus obtaining a supply of cholesterol (see chapter 3, p. 77).

While LDL delivers cholesterol to tissues, HDL (high-density lipoprotein with a high concentration of protein and a low concentration of lipids) removes cholesterol from tissues. The liver produces the basic HDL framework and secretes the HDL molecules into the bloodstream. As they circulate, the HDL molecules pick up cholesterol from peripheral tissues and return to the liver, where they enter liver cells by receptor-mediated endocytosis. The liver disposes of the cholesterol it obtains in this manner by secreting it into bile or by using it to synthesize bile salts.

The intestine reabsorbs much of the cholesterol and bile salts in bile, which are then transported back to the liver, and the secretion-reabsorption cycle repeats. During each cycle, some of the cholesterol and bile salts escape reabsorption, reach the large intestine, and are excreted as part of the feces.

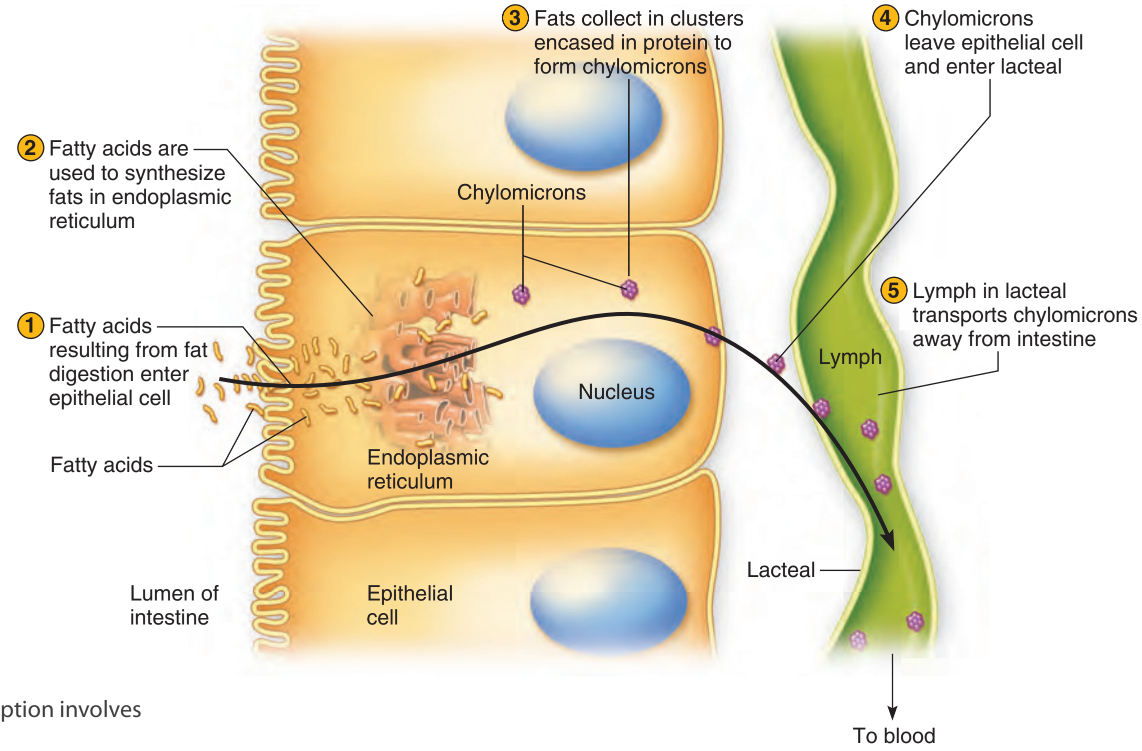

③ Fats collect in clusters encased in protein to form chylomicrons
④ Chylomicrons leave epithelial cell and enter lacteal
② Fatty acids are used to synthesize fats in endoplasmic reticulum
Chylomicrons
① Fatty acids resulting from fat digestion enter epithelial cell
⑤ Lymph in lacteal transports chylomicrons away from intestine
Lymph
Nucleus
Fatty acids
Endoplasmic reticulum
Lacteal
Lumen of intestine
Epithelial cell
To blood

**FIGURE 15.26** Fat absorption involves several steps.

In addition to the products of carbohydrate, protein, and fat digestion, the intestinal villi absorb electrolytes by diffusion and active transport and water by osmosis. Table 15.6 summarizes the absorption process.

**PRACTICE**

38. Which substances resulting from digestion of carbohydrate, protein, and fat molecules does the small intestine absorb?
39. Describe how fatty acids are absorbed and transported.

In *malabsorption,* the small intestine does not absorb some nutrients. Symptoms of malabsorption include diarrhea, weight loss, weakness, vitamin deficiencies, anemia, and bone demineralization. Causes of malabsorption include surgical removal of a portion of the small intestine, obstruction of lymphatic vessels due to a tumor, interference with the production and release of bile as a result of liver disease, or enzyme deficiency.

Another cause of malabsorption is a reaction to *gluten.* Gluten is a composite of two types of proteins that are found in certain grains, such as wheat, barley, and rye. This condition, called *celiac disease*, damages or even destroys microvilli, reducing the surface area of the small intestine, preventing adequate absorption of some nutrients. Some grocery stores and restaurants offer a variety of gluten-free products.

## Movements of the Small Intestine

The small intestine carries on mixing movements and peristalsis, like the stomach. The major mixing movement is segmentation, in which periodic small, ringlike contractions cut chyme into segments and move it back and forth. Segmentation also slows the movement of chyme through the small intestine.

Weak peristaltic waves propel chyme short distances through the small intestine. Consequently, chyme moves slowly through the small intestine, taking from three to ten hours to travel its length.

If the small intestine wall becomes overdistended or irritated, a strong *peristaltic rush* may pass along the organ's entire length. This movement sweeps the contents of the small intestine into the large intestine so quickly that water, nutrients, and electrolytes that would normally be absorbed are not. The result is *diarrhea,* characterized by more frequent defecation and watery stools. Prolonged diarrhea causes imbalances in water and electrolyte concentrations.

At the distal end of the small intestine, the **ileocecal** (il″e-o-se′kal) **sphincter** joins the small intestine's ileum to the large intestine's cecum (fig. 15.27). Normally, this sphincter remains constricted, preventing the contents of the small intestine from entering the large intestine, and the contents of the large intestine from backing up into the ileum. However, after a meal, a gastroileal reflex increases peristalsis in the ileum and relaxes the sphincter, forcing some of the contents of the small intestine into the cecum.

**PRACTICE**

40. Describe the movements of the small intestine.
41. What is a peristaltic rush?

## 15.10 | Large Intestine

The **large intestine** is so named because its diameter is greater than that of the small intestine. This part of the alimentary canal is about 1.5 meters long. It begins in the lower right side of the abdominal cavity, where the ileum joins the cecum. From there, the large intestine ascends on the right side, crosses obliquely to the left, and descends into the pelvis. At its distal end, it opens to the outside of the body as the anus (see fig. 15.1).

The large intestine absorbs water and electrolytes from chyme remaining in the alimentary canal. It also forms and stores feces.

**TABLE 15.6 Intestinal Absorption of Nutrients**

| Nutrient | Absorption Mechanism | Means of Circulation |
|---|---|---|
| Monosaccharides | Facilitated diffusion and active transport | Blood in capillaries |
| Amino acids | Active transport | Blood in capillaries |
| Fatty acids and glycerol | Facilitated diffusion of glycerol; diffusion of fatty acids into cells or blood capillaries | |
| | (a) Most fatty acids are resynthesized into fats and incorporated in chylomicrons | Lymph in lacteals |
| | (b) Some fatty acids with relatively short carbon chains are absorbed without being changed back into fats | Blood in capillaries |
| Electrolytes | Diffusion and active transport | Blood in capillaries |
| Water | Osmosis | Blood in capillaries |

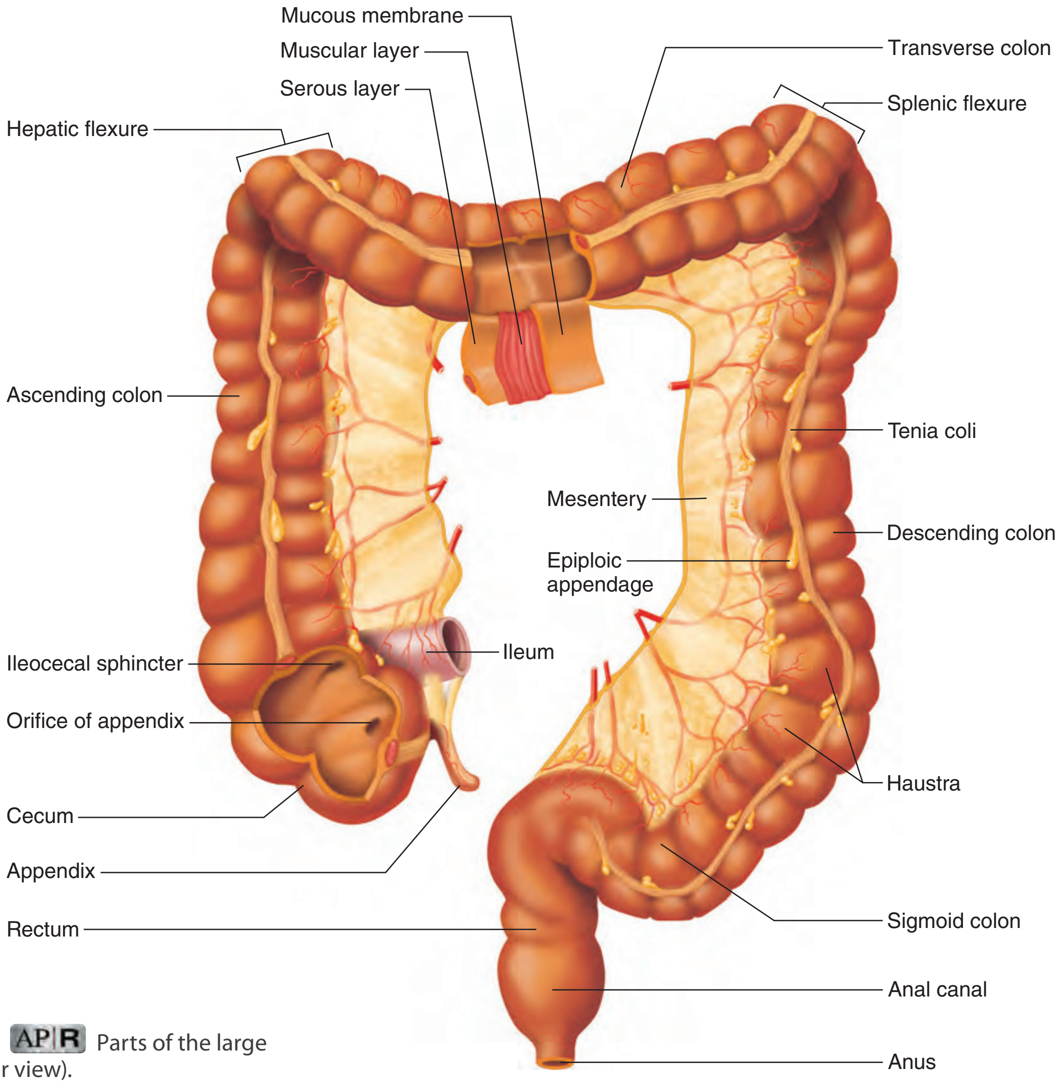

Mucous membrane
Muscular layer
Serous layer
Transverse colon
Splenic flexure
Hepatic flexure
Ascending colon
Tenia coli
Mesentery
Descending colon
Epiploic appendage
Ileum
Ileocecal sphincter
Orifice of appendix
Haustra
Cecum
Appendix
Sigmoid colon
Rectum
Anal canal
Anus

**FIGURE 15.27** APR Parts of the large intestine (anterior view).

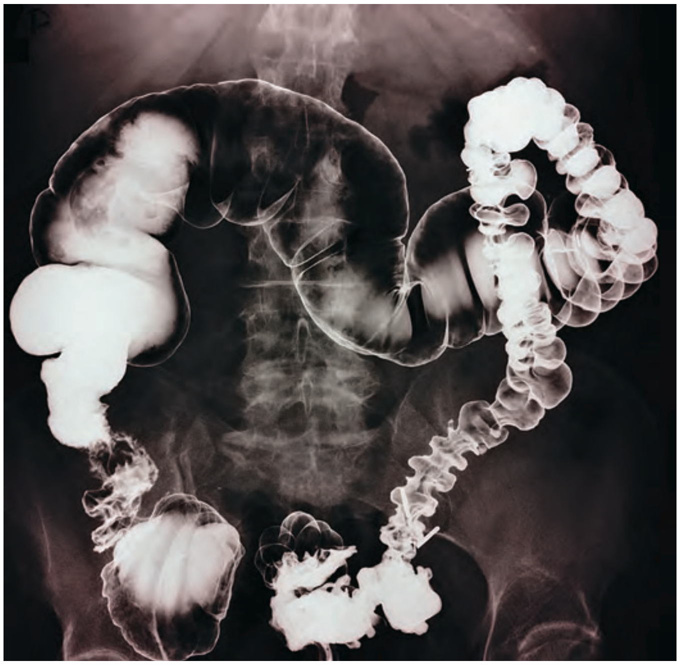


**FIGURE 15.28** Radiograph of the large intestine containing a radiopaque substance that the patient ingested.

## Parts of the Large Intestine

The large intestine consists of the cecum, colon, rectum, and anal canal (figs. 15.27 and 15.28; see reference plates 4 and 5, pp. 35–36). The **cecum,** at the beginning of the large intestine, is a dilated, pouchlike structure that hangs slightly below the ileocecal opening. Projecting downward from it is a closed end, narrow tube containing lymphatic tissue called the **appendix.** The human appendix has no known digestive function.

In *appendicitis,* the appendix becomes inflamed and infected. Surgery is often required to remove the appendix before it ruptures. If it does rupture, this may allow contents of the large intestine to enter the abdominal cavity and cause a serious inflammation of the peritoneum called *peritonitis.*

Removal of the appendix raises the risk of recurrence of certain infections, such as *Clostridium difficile.* This evidence suggests that the human appendix, once thought to have no function, may be a storage place for the healthy "gut microbiome" (see opening vignette, page 410).

The **colon** is divided into four parts—the ascending, transverse, descending, and sigmoid colons. The **ascending colon** begins at the cecum and continues upward against the posterior abdominal wall to a point just inferior to the liver. There, it turns sharply to the left and becomes the **transverse colon.** The transverse colon is the longest and most movable part of the large intestine. It is suspended by a fold of peritoneum and sags in the middle below the stomach. As the transverse colon approaches the spleen, it turns abruptly downward and becomes the **descending colon.** At the brim of the pelvis, the descending colon makes an S-shaped curve called the **sigmoid colon** and then becomes the rectum.

The **rectum** lies next to the sacrum and generally follows its curvature. The peritoneum firmly attaches the rectum to the sacrum, and the rectum ends about 5 centimeters below the tip of the coccyx, where it becomes the anal canal (see fig. 15.27).

The last 2.5–4.0 centimeters of the large intestine form the **anal canal** (fig. 15.29). The mucous membrane in the canal is folded into six to eight longitudinal *anal columns.* At its distal end, the canal opens to the outside as the **anus.** Two sphincter muscles guard the anus—an *internal anal sphincter muscle,* composed of smooth muscle under involuntary control, and an *external anal sphincter muscle,* composed of skeletal muscle under voluntary control.

## PRACTICE

42. What is the general function of the large intestine?
43. Describe the parts of the large intestine.

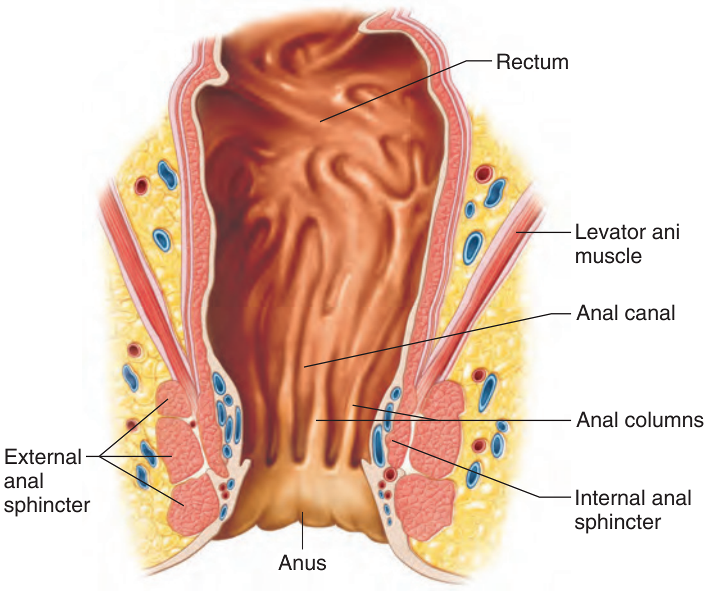


**FIGURE 15.29** The rectum and the anal canal are at the distal end of the alimentary canal.

*Hemorrhoids* are enlarged and inflamed branches of the rectal vein in the anal columns that cause intense itching, sharp pain, and sometimes bright red bleeding. The hemorrhoids may be internal or bulge out of the anus (external). Causes of hemorrhoids include anything that puts prolonged pressure on the delicate rectal tissue, including obesity, pregnancy, constipation, diarrhea, and liver disease.

## Structure of the Large Intestinal Wall

The wall of the large intestine is composed of the same types of tissues as other parts of the alimentary canal but also has unique features. The large intestinal wall does not have the villi characteristic of the small intestine, and the layer of longitudinal muscle fibers is not uniformly distributed throughout the large intestinal wall. Instead, the fibers form three distinct bands (teniae coli) that extend the entire length of the colon (see fig. 15.27). These bands exert tension lengthwise on the wall, creating a series of pouches (haustra).

Fiberoptic colonoscopy is a test commonly performed on people over age 50, when the risk of colorectal cancer increases. Under sedation, a flexible lit tube is inserted into the rectum, and polyps and tumors are identified and removed. Computed tomographic colonography (popularly called a virtual colonoscopy) requires the same preparatory bowel cleansing, but does not require sedation and is faster. However, if a lesion is detected, the more invasive fiberoptic colonoscopy must be used to remove the suspicious tissue.

## Functions of the Large Intestine

The large intestine has little or no digestive function, in contrast to the small intestine, which secretes digestive enzymes and absorbs the products of digestion. However, the mucous membrane that forms the large intestine's inner lining contains many tubular glands. Structurally, these glands are similar to those of the small intestine, but they are composed almost entirely of goblet cells (fig. 15.30). Consequently, mucus is the large intestine's only significant secretion.

Mucus secreted into the large intestine protects the intestinal wall against the abrasive action of the materials passing through it. Mucus also binds particles of fecal matter, and its alkalinity helps control the pH of the large intestinal contents.

Chyme entering the large intestine contains materials that the small intestine did not digest or absorb. It also contains water, electrolytes, mucus, and bacteria. The large intestine normally absorbs water (although most water is absorbed in the small intestine) and electrolytes in the proximal half of the tube. Substances that remain in the tube become feces and are stored in the distal part of the large intestine.

The many bacteria that normally inhabit the large intestine, called *intestinal flora,* break down some of the molecules that escape the actions of human digestive enzymes. For instance, cellulose, a complex carbohydrate in food of plant origin, passes through the alimentary canal almost unchanged, but colon bacteria can break down cellulose and use it as an energy source. These bacteria, in turn, synthesize certain vitamins, such as K, $B_{12}$, thiamine, and riboflavin, which the intestinal mucosa absorbs. Bacterial actions in the large intestine may produce intestinal gas (flatus).

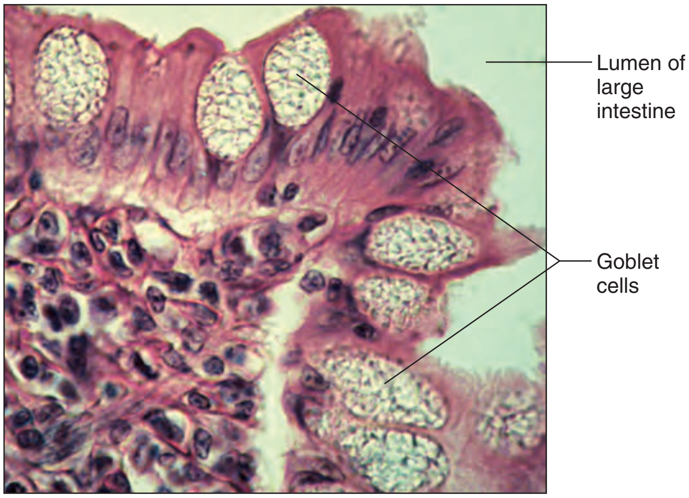


**FIGURE 15.30** APR Light micrograph of the large intestinal mucosa (560×).

Q *Note the many goblet cells in the mucosa of the large intestine. Why are there so many more of these cells in the large intestinal wall than in the small intestinal wall?*

**Answer can be found in Appendix F on page 582.**

### PRACTICE

44. How does the structure of the large intestine differ from that of the small intestine?
45. Which substances does the large intestine absorb?

## Movements of the Large Intestine

The movements of the large intestine—mixing and peristalsis—are similar to those of the small intestine, although usually slower. Also, peristaltic waves of the large intestine happen only two or three times each day. These waves produce *mass movements* in which a large section of the intestinal wall constricts vigorously, forcing the intestinal contents toward the rectum. Typically, mass movements follow a meal as a result of the gastrocolic reflex initiated in the small intestine. Irritations of the intestinal mucosa also can trigger such movements. For instance, a person with an inflamed colon (colitis) may experience frequent mass movements. Clinical Application 15.3 discusses inflammatory bowel disease.

A person can usually initiate a *defecation reflex* by holding a deep breath and contracting the abdominal wall muscles. This action increases internal abdominal pressure and forces feces into the rectum. As the rectum fills, its wall distends, triggering the defecation reflex that stimulates peristaltic waves in the descending colon. The internal anal sphincter relaxes. At the same time, other reflexes involving the sacral region of the spinal cord strengthen the peristaltic waves, lower the diaphragm, close the glottis, and contract the abdominal wall muscles. These actions further increase internal abdominal pressure and squeeze the rectum. The external anal sphincter is signaled to relax, and the feces are forced to the outside. Contracting the external anal sphincter allows voluntary inhibition of defecation.

## Feces

**Feces** (fe′sēz) include materials not digested or absorbed, plus water, electrolytes, mucus, shed intestinal cells, and bacteria. Usually, feces are about 75% water, and their color derives from bile pigments altered by bacterial action. Feces' pungent odor results from a variety of compounds that bacteria produce.

### PRACTICE

46. How does peristalsis in the large intestine differ from peristalsis in the small intestine?
47. List the major events of defecation.
48. Describe the composition of feces.

CLINICAL APPLICATION 15.3

### Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a group of disorders that affect about a million people in the United States. The most common ages of onset are between ten and thirty years, and between fifty and sixty years. IBD includes ulcerative colitis and Crohn's disease. These disorders differ by the site and extent of inflammation and ulceration of the intestines. Both produce abdominal cramps and diarrhea.

IBD is usually the result of an inflammatory response, such as to infection, that does not stop. About 10–20% of people with IBD have relatives with the condition. Mutations in several genes cause severe IBD in young children. The genes normally encode receptors for cytokines that halt the inflammatory response. When mutations impair the receptors so that inflammation stays on, painfully swollen intestines result.

Ulcerative colitis affects the mucosa and submucosa of the distal large intestine and the rectum. In about 25% of cases, the disease extends no farther than the rectum. Bloody diarrhea and cramps may last for days or weeks, and vary in frequency. The severe diarrhea leads to weight loss and electrolyte imbalances and may affect other organs, including the skin, eyes, or liver. The inflamed and ulcerous tissue is continuous. Severe ulcerative colitis is also associated with increased risk of developing colon cancer.

Crohn's disease is more extensive than ulcerative colitis, infiltrating the small and large intestines and penetrating all tissue layers. In contrast to the uniformity of ulcerative colitis, affected portions of intestine in Crohn's disease are interspersed with unaffected areas, producing a "cobblestone" effect after many years. Rarely, the disease affects more proximal structures of the gastrointestinal tract. The diarrhea is often not bloody, and complications such as cancer are rare.

Several classes of drugs are used to control IBD. They affect different parts of the gastrointestinal tract and/or different parts of the immune response that contribute to the excess inflammation. Surgery may be necessary if drug therapy is ineffective or if cancer develops. For at least one very severe type of IBD that is inherited and primarily affects the immune system, a bone marrow or stem cell transplant can be life-saving.

## 15.11 | Nutrition and Nutrients

Nutrition is the study of nutrients and how the body utilizes them. **Nutrients** (nu′tre-ents) are chemicals supplied from the environment that an organism requires for survival, and include carbohydrates, lipids, proteins, vitamins, minerals, and water (see chapter 2, pp. 49–55, and chapter 4, p. 92). Carbohydrates, lipids, and proteins are called **macronutrients** because they are required in large amounts. They provide energy as well as other specific functions. Vitamins and minerals are required in much smaller amounts and are therefore called **micronutrients.** They do not directly provide energy, but make possible the biochemical reactions that extract energy from macronutrient molecules.

Macronutrients provide potential energy that can be expressed in calories, which are units of heat. A **calorie** (kal′o-re) is the amount of heat required to raise the temperature of a gram of water by 1° Celsius. The calorie used to measure food energy is 1,000 times greater. This larger calorie (Cal) is technically a kilocalorie, but nutritional studies commonly refer to it simply as a calorie. As a result of cellular oxidation, 1 gram of carbohydrate or 1 gram of protein yields on average about 4.1 calories, and 1 gram of fat yields about 9.5 calories (more than twice as much chemical energy as carbohydrates or proteins).

Foods provide nutrients, and digestion breaks nutrients down to sizes that can be absorbed and transported in the bloodstream. Nutrients that human cells cannot synthesize, such as certain amino acids, are called **essential nutrients.**

**PRACTICE**

49. Identify and distinguish among macronutrients and micronutrients.
50. How is food energy measured?

### Carbohydrates

**Carbohydrates** are organic compounds and include the sugars and starches. The energy held in their chemical bonds is used primarily to power cellular processes.

#### *Carbohydrate Sources*

Carbohydrates are ingested in a variety of forms, including starch from grains and vegetables; glycogen from meats; disaccharides from milk sugar, cane sugar, beet sugar, and molasses; and monosaccharides from honey and fruits (see chapter 2, pp. 49–50). Digestion breaks down complex carbohydrates into monosaccharides, which are small enough to be absorbed into the bloodstream.

*Cellulose* is a complex carbohydrate that is abundant in food—it gives celery its crunch and lettuce its crispness. Humans cannot digest cellulose, so the portion of it that is not broken down by intestinal flora passes through the alimentary canal largely unchanged. In this way, cellulose provides bulk (also called fiber or roughage) against which the muscular wall of the digestive system can push, easing the movement of intestinal contents.

### Carbohydrate Use

The monosaccharides absorbed from the digestive tract include *fructose, galactose,* and *glucose.* Liver enzymes catalyze reactions that convert fructose and galactose into glucose, which is the carbohydrate form most commonly oxidized for cellular fuel (see chapter 4, pp. 91–92).

Many cells obtain energy by oxidizing fatty acids. Some cells, however, such as neurons, normally require a continuous supply of glucose for survival. Even a temporary decrease in the glucose supply may seriously impair nervous system function. Consequently, the body requires a minimum amount of carbohydrates. If foods do not provide an adequate carbohydrate supply, the liver may convert some noncarbohydrates, such as amino acids from proteins, into glucose. The requirement for glucose has physiological priority over the requirement to synthesize proteins from available amino acids.

Carbohydrates have functions other than providing energy. Some excess glucose is polymerized to form *glycogen,* which is stored in the liver and muscles. When glucose is required to supply energy, it can be mobilized rapidly by breaking down glycogen. However, the body can store only a certain amount of glycogen, so excess glucose is usually converted into fat and stored in adipose tissue. To obtain energy, the body first metabolizes glucose, then glycogen stores, and finally fats and proteins.

Cells use carbohydrates as starting materials for synthesizing such vital biochemicals as the five-carbon sugars *ribose* and *deoxyribose,* required for production of the nucleic acids RNA and DNA. Carbohydrates are also required to synthesize the disaccharide *lactose* (milk sugar) when the breasts are actively secreting milk.

### Carbohydrate Requirements

Carbohydrates provide the primary fuel source for cellular processes, so the need for carbohydrates varies with individual energy expenditure. Physically active individuals require more fuel than those who are sedentary. The minimal requirement for carbohydrates in the human diet is unknown. It is estimated, however, that an intake of at least 125 to 175 grams daily is necessary to avoid protein breakdown and to avoid metabolic disorders resulting from excess fat use.

**PRACTICE**

51. List several common sources of carbohydrates.
52. Explain the importance of cellulose in the diet.
53. Explain why the requirement for glucose has priority over protein synthesis.
54. Why do daily requirements for carbohydrates vary from person to person?

## Lipids

**Lipids** are organic compounds that include fats, oils, and fatlike substances such as phospholipids and cholesterol. They supply energy for cellular processes and help build structures, such as cell membranes. The most common dietary lipids are the fats called *triglycerides.* Recall from chapter 2 (p. 51) that a triglyceride molecule consists of a glycerol and three fatty acids.

### Lipid Sources

Triglycerides are found in plant- and animal-based foods. Saturated fats are mainly found in foods of animal origin, such as meats, eggs, milk, and lard, as well as in palm and coconut oils. Unsaturated fats are in seeds, nuts, and plant oils. Monounsaturated fats, such as those in olive, peanut, and canola oils, are the healthiest. Saturated fats in excess are a risk factor for cardiovascular disease.

*Cholesterol* is abundant in liver and egg yolk and, to a lesser extent, in whole milk, butter, cheese, and meats. It is not present in foods of plant origin.

### Lipid Use

The lipids in foods are phospholipids, cholesterol, or triglycerides. Lipids provide a variety of physiological functions; however, fats mainly supply energy. Before a triglyceride molecule can release energy, it must undergo hydrolysis (breakdown in the presence of water) as part of digestion, releasing the constituent fatty acids and glycerol. After being absorbed, these products are transported in lymph to the blood, then on to tissues. Figure 15.31 shows that some of the fatty acid portions can react to form molecules of acetyl coenzyme A by a series of reactions called **beta oxidation** (ba′tah ok″sĭ-da′shun). Excess acetyl coenzyme A can be converted into compounds called *ketone bodies,* such as acetone, which later may be changed back to acetyl coenzyme A. In either case, the resulting acetyl coenzyme A can be oxidized in the citric acid cycle. The glycerol parts of the triglyceride molecules can also enter metabolic pathways leading

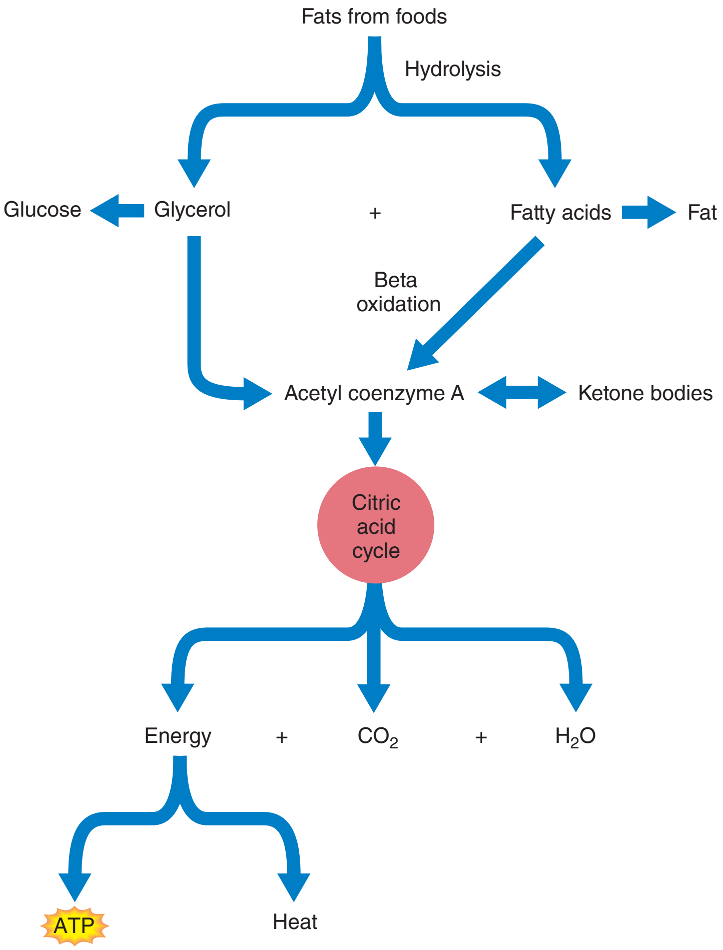


**FIGURE 15.31** The body digests fats from foods into glycerol and fatty acids, which may enter catabolic pathways and provide energy.

to the citric acid cycle, or they can be used to synthesize glucose. Fatty acid molecules released from fat hydrolysis can combine to form fat molecules and be stored in adipose tissue.

The liver can convert fatty acids from one form to another, but it cannot synthesize certain fatty acids, called **essential fatty acids.** *Linoleic acid,* for example, is required for phospholipid synthesis, which in turn is necessary for constructing cell membranes and myelin sheaths, and transporting circulating lipids. Good sources of linoleic acid include corn, cottonseed, and soy oils. Another essential fatty acid is *linolenic acid.*

The liver regulates circulating lipids by using free fatty acids to synthesize triglycerides, phospholipids, and lipoproteins that may then be released into the bloodstream. Because lipids are less dense than proteins, as the proportion of lipids in a lipoprotein increases, the density of the particle decreases. Conversely, as the proportion of lipids decreases, the density increases. Lipoproteins are classified on the basis of their densities, which reflect their composition. *Very-low-density lipoproteins* (VLDL) have a relatively high concentration of triglycerides. *Low-density lipoproteins* (LDL) have a relatively high concentration of cholesterol and are the major cholesterol-carrying lipoproteins. *High-density lipoproteins* (HDL) have a relatively high concentration of protein and a lower concentration of lipids.

In addition to regulating circulating lipids, the liver controls the total amount of cholesterol in the body by synthesizing cholesterol and releasing it into the blood, or by removing cholesterol from the blood and excreting it into bile. The liver also uses cholesterol to produce bile salts. Cholesterol is not an energy source. It provides structural material for cell and organelle membranes and it furnishes starting material for the synthesis of certain sex hormones and adrenal cortex hormones.

Adipose tissue stores excess triglycerides. If the blood lipid concentration drops (in response to fasting, for example), some of these triglycerides are hydrolyzed into free fatty acids and glycerol, and then released into the bloodstream.

### *Lipid Requirements*

The amounts and types of fats required for health vary with individuals' habits and goals. Because linoleic acid is an essential fatty acid, nutritionists recommend that formula-fed infants receive 3% of their energy intake in the form of linoleic acid to prevent deficiency conditions. Fat intake must be sufficient to carry fat-soluble vitamins. Lipids provide flavor to food, which is one reason why adhering to a very low-fat diet is difficult. The USDA and American Heart Association recommend that lipid intake not exceed 30% of the total daily calories.

**PRACTICE**

55. Which fatty acids are essential nutrients?
56. What is the liver's role in the use of lipids?
57. What are the functions of cholesterol?

## Proteins

**Proteins** are composed of amino acids. They have a wide variety of functions.

### *Protein Sources*

Foods rich in proteins include meats, seafood, poultry, cheese, nuts, milk, eggs, and cereals. Legumes, including beans and peas, contain less protein. The cells of an adult can synthesize all but eight required amino acids, and the cells of a child can produce all but ten. Amino acids that the body can synthesize are termed nonessential; those that the body cannot synthesize and must obtain from the diet are **essential amino acids.** Table 15.7 lists the amino acids in foods and indicates those that are essential.

**TABLE 15.7 Amino Acids in Foods**

- Alanine
- Arginine (ch)
- Asparagine
- Aspartic acid
- Cysteine
- Glutamic acid
- Glutamine
- Glycine
- Histidine (ch)
- Isoleucine (e)
- Leucine (e)
- Lysine (e)
- Methionine (e)
- Phenylalanine (e)
- Proline
- Serine
- Threonine (e)
- Tryptophan (e)
- Tyrosine
- Valine (e)

Eight essential amino acids (e) cannot be synthesized by human cells and must be provided in the diet. Two additional amino acids (ch) are essential in growing children.

All twenty types of amino acids must be in the body at the same time for growth and tissue repair to occur, because many proteins include all twenty types of amino acids. Therefore, if just one type of essential amino acid is missing from the diet, normal protein synthesis cannot take place.

Proteins are classified as complete or incomplete on the basis of the amino acid types they provide. **Complete proteins,** such as those in milk, meats, and eggs, have adequate amounts of the essential amino acids. **Incomplete proteins,** such as *zein* in corn, which has too little of the essential amino acids tryptophan and lysine, are unable by themselves to maintain human tissues or to support normal growth and development. A protein in wheat called *gliadin* is a **partially complete protein** because it has very little of the amino acid lysine.

Many plant proteins have too little of one or more essential amino acids to provide adequate nutrition for a person. However, combining appropriate plant foods can supply an adequate diversity of dietary amino acids. For example, beans are low in methionine but have enough lysine. Rice lacks lysine but has enough methionine. A meal of beans and rice provides enough of both types of amino acids.

## *Protein Use*

When dietary proteins are digested, the resulting amino acids are absorbed and transported by the blood to the cells, which use the amino acids to synthesize proteins. These new proteins include enzymes that control the rates of metabolic reactions, clotting factors, the keratin of skin and hair, elastin and collagen of connective tissue, plasma proteins that regulate water balance, the muscle components actin and myosin, certain hormones, and the antibodies that protect against infection.

Proteins may also supply energy after digestion breaks them down into amino acids. The liberated amino acids are transported to the liver, where they undergo *deamination,* losing their nitrogen-containing ($-NH_2$) groups (see fig. 2.17, p. 53). These $-NH_2$ groups subsequently react to form the waste *urea* (u-re′ah), which is excreted in urine.

Depending upon the particular amino acids involved, the remaining deaminated parts are decomposed in one of several pathways (fig. 15.32). Some of these pathways lead to formation of acetyl coenzyme A, and others lead more directly to the steps of the citric acid cycle. As energy is released from the cycle, some of it is captured in ATP molecules. If energy is not required immediately, the deaminated parts of the amino acids may react to form glucose or fat molecules in other metabolic pathways.

## *Protein Requirements*

Proteins supply essential amino acids. They also provide nitrogen and other elements for the synthesis of nonessential amino acids and certain nonprotein nitrog-

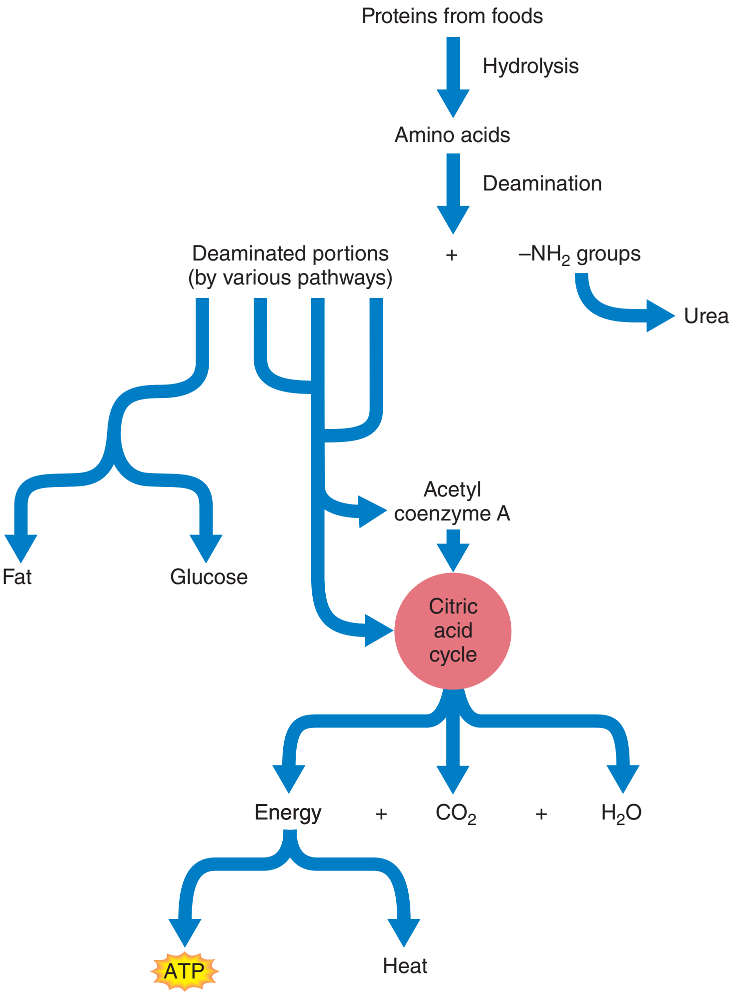


**FIGURE 15.32** The body digests proteins from foods into amino acids, but must deaminate these smaller molecules before they can be used as energy sources.

enous substances. The amount of dietary protein individuals require varies according to body size, metabolic rate, and other factors, such as activity level. Bodybuilders, for example, require more protein to help heal small muscle tears that result from weight lifting.

For an average adult, nutritionists recommend a daily protein intake of about 0.8 grams per kilogram of body weight. Another way to estimate desirable protein intake is to divide weight in pounds by two. Most people should consume 60 to 150 grams of protein a day. For a pregnant woman, the recommendation adds 30 grams of protein per day. Similarly, a nursing mother requires an additional 20 grams of protein per day to maintain milk production.

### PRACTICE

58. Which foods are rich sources of proteins?
59. Why are some amino acids called essential?
60. Distinguish between complete and incomplete proteins.
61. List some examples of proteins associated with the body.
62. How does dietary protein provide energy?

## Vitamins

**Vitamins** (vi′tah-minz) are organic compounds (other than carbohydrates, lipids, and proteins) required in small amounts for normal metabolism, that cells cannot synthesize in adequate amounts. Therefore, they are essential nutrients that must come from foods.

Vitamins are classified on the basis of solubility. Some are soluble in fats (or fat solvents) and others are soluble in water. *Fat-soluble vitamins* are vitamins A, D, E, and K; *water-soluble vitamins* are the B vitamins and vitamin C.

### *Fat-Soluble Vitamins*

Fat-soluble vitamins dissolve in fats, and therefore they associate with lipids and respond to the same factors that affect lipid absorption. For example, bile salts in the intestine promote absorption of these vitamins. Fat-soluble vitamins accumulate in various tissues, which is why excess intake can lead to overdose conditions. For example, too much beta carotene, a vitamin A precursor, can tinge the skin orange. Fat-soluble vitamins resist the effects of heat; therefore, cooking and food processing usually do not destroy them. Table 15.8 lists the fat-soluble vitamins and their characteristics, functions, sources, and recommended daily allowances (RDAs) for adults.

### *Water-Soluble Vitamins*

The water-soluble vitamins include the B vitamins and vitamin C. The **B vitamins** are several compounds that are essential for normal cellular metabolism. They help oxidize carbohydrates, lipids, and proteins. The B vitamins are usually in the same foods, so they are called the *vitamin B complex.* Members of this group differ chemically and functionally. Cooking and food processing destroy some of them.

**Vitamin C** (ascorbic acid) is one of the least stable vitamins and is fairly widespread in plant foods. It is necessary for collagen production, the conversion of folacin to folinic acid, and the metabolism of certain amino acids. Vitamin C also promotes iron absorption and synthesis of certain hormones from cholesterol. Table 15.9 lists the water-soluble vitamins and their characteristics, functions, sources, and RDAs for adults.

**TABLE 15.8 Fat-Soluble Vitamins**

| Vitamin | Characteristics | Functions | Sources and RDA[*] for Adults |
|---|---|---|---|
| Vitamin A | Exists in several forms; synthesized from carotenes; stored in liver; stable in heat, acids, and bases; unstable in light | An antioxidant necessary for synthesis of visual pigments, mucoproteins, and mucopolysaccharides; for normal development of bones and teeth; and for maintenance of epithelial cells | Liver, fish, whole milk, butter, eggs, leafy green vegetables, yellow and orange vegetables and fruits; RDA = 4,000–5,000 IU[†] |
| Vitamin D | A group of steroids; resistant to heat, oxidation, acids, and bases; stored in liver, skin, brain, spleen, and bones | Promotes absorption of calcium and phosphorus; promotes development of teeth and bones | Produced in skin exposed to ultraviolet light; in milk, egg yolk, fish liver oils, fortified foods; RDA = 400 IU |
| Vitamin E | A group of compounds; resistant to heat and visible light; unstable in presence of oxygen and ultraviolet light; stored in muscles and adipose tissue | An antioxidant; prevents oxidation of vitamin A and polyunsaturated fatty acids; may help maintain stability of cell membranes | Oils from cereal seeds, salad oils, margarine, shortenings, fruits, nuts, and vegetables; RDA = 30 IU |
| Vitamin K | Exists in several forms; resistant to heat, but destroyed by acids, bases, and light; stored in liver | Required for synthesis of prothrombin, which functions in blood clotting | Leafy green vegetables, egg yolk, pork liver, soy oil, tomatoes, cauliflower; RDA = 55–70 $\mu$g |

[*] RDA = recommended daily allowance.

[†] IU = international unit.

**FACTS OF LIFE** Sailors on English ships ate limes to protect them from scurvy (vitamin C deficiency). American ships carried cranberries for the same purpose.

## PRACTICE

63. What are vitamins?
64. How are vitamins classified?
65. How do bile salts affect the absorption of fat-soluble vitamins?
66. List the fat-soluble and water-soluble vitamins.

## Minerals

Dietary **minerals** (min′er-alz) are inorganic elements essential in human metabolism. Plants usually extract these elements from soil, and humans obtain them from plant foods or from animals that have eaten plants.

### *Characteristics of Minerals*

Minerals contribute about 4% of body weight and are most concentrated in the bones and teeth. Many minerals are incorporated into organic molecules. For example, phosphorus is found in phospholipids, iron in hemoglobin, and iodine in thyroxine. However, some minerals are part of inorganic compounds, such as the calcium phosphate of bone. Other minerals are free ions, such as sodium, chloride, and calcium ions in blood.

**TABLE 15.9 Water-Soluble Vitamins**

| Vitamin | Characteristics | Functions | Sources and RDA* for Adults |
|---|---|---|---|
| Thiamine (vitamin $B_1$) | Destroyed by heat and oxygen, especially in alkaline environment | Part of coenzyme required for oxidation of carbohydrates; coenzyme required for ribose synthesis | Lean meats, liver, eggs, whole-grain cereals, leafy green vegetables, legumes; RDA =1.5 mg |
| Riboflavin (vitamin $B_2$) | Stable to heat, acids, and oxidation; destroyed by bases and ultraviolet light | Part of enzymes and coenzymes required for oxidation of glucose and fatty acids and for cellular growth | Meats, dairy products, leafy green vegetables, whole-grain cereals; RDA = 1.7 mg |
| Niacin (nicotinic acid) (vitamin $B_3$) | Stable to heat, acids, and bases; converted to niacinamide by cells; synthesized from tryptophan | Part of coenzymes required for oxidation of glucose and synthesis of proteins, fats, and nucleic acids | Liver, lean meats, peanuts, legumes; RDA = 20 mg |
| Pantothenic acid (vitamin $B_5$) | Destroyed by heat, acids, and bases | Part of coenzyme A required for oxidation of carbohydrates and fats | Meats, whole-grain cereals, legumes, milk, fruits, vegetables; RDA = 10 mg |
| Vitamin $B_6$ | Group of three compounds; stable to heat and acids; destroyed by oxidation, bases, and ultraviolet light | Coenzyme required for synthesis of proteins and certain amino acids, for conversion of tryptophan to niacin, for production of antibodies, and for nucleic acid synthesis | Liver, meats, bananas, avocados, beans, peanuts, whole-grain cereals, egg yolk; RDA = 2 mg |
| Biotin (vitamin $B_7$) | Stable to heat, acids, and light; destroyed by oxidation and bases | Coenzyme required for metabolism of amino acids and fatty acids, and for nucleic acid synthesis | Liver, egg yolk, nuts, legumes, mushrooms; RDA = 0.3 mg |
| Folacin (folic acid) (vitamin $B_9$) | Occurs in several forms; destroyed by oxidation in acid environment or by heat in alkaline environment; stored in liver, where it is converted into folinic acid | Coenzyme required for metabolism of certain amino acids and for DNA synthesis; promotes production of normal red blood cells | Liver, leafy green vegetables, whole-grain cereals, legumes; RDA = 0.4 mg |
| Cyanocobalamin (vitamin $B_{12}$) | Complex, cobalt-containing compound; stable to heat; inactivated by light, strong acids, and strong bases; absorption regulated by intrinsic factor from gastric glands; stored in liver | Part of coenzyme required for synthesis of nucleic acids and for metabolism of carbohydrates; plays role in myelin synthesis; needed for normal red blood cell production | Liver, meats, milk, cheese, eggs; RDA = 3–6 $\mu$g |
| Ascorbic acid (vitamin C) | Chemically similar to monosaccharides; stable in acids but destroyed by oxidation, heat, light, and bases | Required for collagen production, conversion of folacin to folinic acid, and metabolism of certain amino acids; promotes absorption of iron and synthesis of hormones from cholesterol | Citrus fruits, tomatoes, potatoes, leafy green vegetables; RDA = 60 mg |

*RDA = recommended daily allowance.

Minerals are parts of the structural materials of all body cells. They also constitute portions of enzyme molecules, contribute to the osmotic pressure of body fluids, and play vital roles in impulse conduction in neurons, muscle fiber contraction, blood coagulation, and maintenance of the pH of body fluids.

### *Major Minerals*

*Calcium* and *phosphorus* account for nearly 75% by weight of the mineral elements in the body. Therefore, they are termed **major minerals.** Other major minerals, each of which accounts for 0.05% or more of the body weight, include potassium, sulfur, sodium, chlorine, and magnesium. Table 15.10 lists the distribution, functions, sources, and adult RDAs of major minerals.

**FACTS OF LIFE** The human body has enough phosphorus to make 2,000 match tips.

### *Trace Elements*

**Trace elements** are essential minerals found in minute amounts, each making up less than 0.005% of adult body weight. They include iron, manganese, copper, iodine, cobalt, zinc, fluorine, selenium, and chromium. Table 15.11 lists the distribution, functions, sources, and adult RDAs of the trace elements.

**FACTS OF LIFE** A human body has enough iron to make a small nail.

**PRACTICE**

67. What are minerals?
68. What are the major functions of minerals?
69. Distinguish between a major mineral and a trace element.
70. Name the major minerals and trace elements.

## Adequate Diets

An *adequate diet* provides sufficient energy (calories), essential fatty acids, essential amino acids, vitamins, and minerals to support optimal growth and to maintain and repair body tissues. Individual requirements for nutrients vary greatly with age, sex, growth rate, physical activity, and level of stress, as well as with genetic and environmental factors. Therefore, designing a diet that is adequate for everyone is impossible. In the past, diagrams called food pyramids were used to organize foods according to suggested relative amounts. Figure 15.33 depicts a replacement design, *My Plate,* more recently developed by the U.S. Department of Agriculture.

**TABLE 15.10 Major Minerals**

| Mineral | Distribution | Functions | Sources and RDA* for Adults |
|---|---|---|---|
| Calcium (Ca) | Mostly in the inorganic salts of bones and teeth | Structure of bones and teeth; essential for neurotransmitter release, muscle fiber contraction, and blood coagulation; increases permeability of cell membranes; activates certain enzymes | Milk, milk products, leafy green vegetables; RDA = 800 mg |
| Phosphorus (P) | Mostly in the inorganic salts of bones and teeth | Structure of bones and teeth; component in nearly all metabolic reactions; in nucleic acids, many proteins, some enzymes, and some vitamins; in cell membrane, ATP, and phosphates of body fluids | Meats, cheese, nuts, whole-grain cereals, milk, legumes; RDA = 800 mg |
| Potassium (K) | Widely distributed; tends to be concentrated inside cells | Helps maintain intracellular osmotic pressure and regulate pH; required for impulse conduction in neurons | Avocados, dried apricots, meats, nuts, potatoes, bananas; RDA = 2,500 mg |
| Sulfur (S) | Widely distributed; abundant in skin, hair, and nails | Essential part of certain amino acids, thiamine, insulin, biotin, and mucopolysaccharides | Meats, milk, eggs, legumes; No RDA established |
| Sodium (Na) | Widely distributed; mostly in extracellular fluids and bound to inorganic salts of bone | Helps maintain osmotic pressure of extracellular fluids; regulates water movement; plays a role in impulse conduction in neurons; regulates pH and transport of substances across cell membranes | Table salt, cured ham, sauerkraut, cheese, graham crackers; RDA = 2,500 mg |
| Chlorine (Cl) | Closely associated with sodium (as chloride); most highly concentrated in cerebrospinal fluid and gastric juice | Helps maintain osmotic pressure of extracellular fluids; regulates pH; maintains electrolyte balance; forms hydrochloric acid; aids transport of carbon dioxide by red blood cells | Same as for sodium; No RDA established |
| Magnesium (Mg) | Abundant in bones | Required in metabolic reactions in mitochondria that produce ATP; plays a role in the breakdown of ATP to ADP | Milk, dairy products, legumes, nuts, leafy green vegetables; RDA = 300–350 mg |

*RDA = recommended daily allowance.

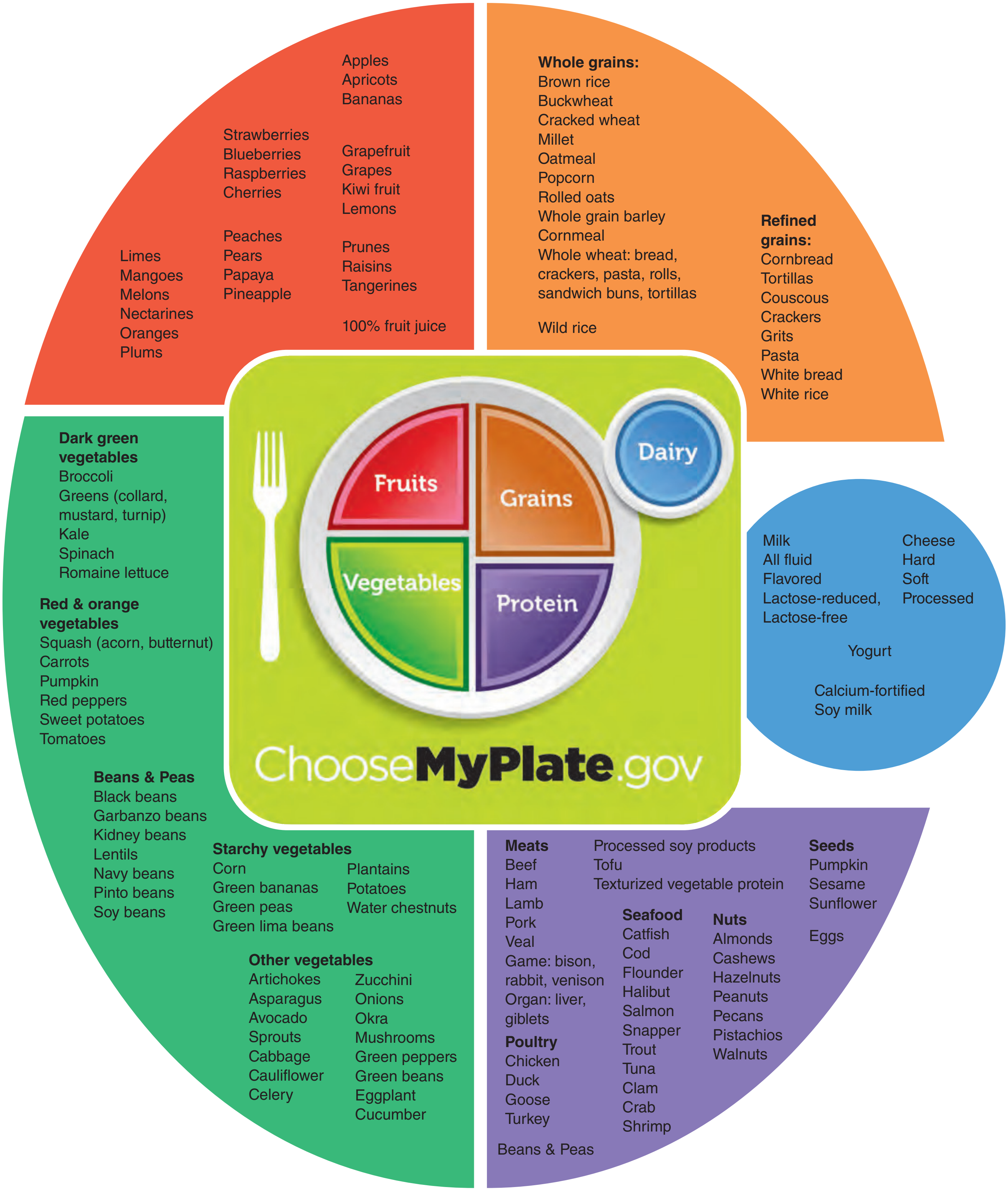

Apples
Apricots
Bananas
Strawberries
Blueberries
Raspberries
Cherries
Grapefruit
Grapes
Kiwi fruit
Lemons
Limes
Mangoes
Melons
Nectarines
Oranges
Plums
Peaches
Pears
Papaya
Pineapple
Prunes
Raisins
Tangerines
100% fruit juice
Whole grains:
Brown rice
Buckwheat
Cracked wheat
Millet
Oatmeal
Popcorn
Rolled oats
Whole grain barley
Cornmeal
Whole wheat: bread, crackers, pasta, rolls, sandwich buns, tortillas
Wild rice
Refined grains:
Cornbread
Tortillas
Couscous
Crackers
Grits
Pasta
White bread
White rice
Fruits
Grains
Dairy
Vegetables
Protein
ChooseMyPlate.gov
Milk
All fluid
Flavored
Lactose-reduced,
Lactose-free
Cheese
Hard
Soft
Processed
Yogurt
Calcium-fortified
Soy milk
Dark green vegetables
Broccoli
Greens (collard, mustard, turnip)
Kale
Spinach
Romaine lettuce
Red & orange vegetables
Squash (acorn, butternut)
Carrots
Pumpkin
Red peppers
Sweet potatoes
Tomatoes
Beans & Peas
Black beans
Garbanzo beans
Kidney beans
Lentils
Navy beans
Pinto beans
Soy beans
Starchy vegetables
Corn
Green bananas
Green peas
Green lima beans
Plantains
Potatoes
Water chestnuts
Other vegetables
Artichokes
Asparagus
Avocado
Sprouts
Cabbage
Cauliflower
Celery
Zucchini
Onions
Okra
Mushrooms
Green peppers
Green beans
Eggplant
Cucumber
Meats
Beef
Ham
Lamb
Pork
Veal
Game: bison, rabbit, venison
Organ: liver, giblets
Poultry
Chicken
Duck
Goose
Turkey
Beans & Peas
Processed soy products
Tofu
Texturized vegetable protein
Seafood
Catfish
Cod
Flounder
Halibut
Salmon
Snapper
Trout
Tuna
Clam
Crab
Shrimp
Nuts
Almonds
Cashews
Hazelnuts
Peanuts
Pecans
Pistachios
Walnuts
Seeds
Pumpkin
Sesame
Sunflower
Eggs

**FIGURE 15.33** My Plate, developed by the U.S. Department of Agriculture, depicts the foods and appropriate proportions that should make up a healthy diet.

**TABLE 15.11** Trace Elements

| Trace Element | Distribution | Functions | Sources and RDA* for Adults |
|---|---|---|---|
| Iron (Fe) | Primarily in blood; stored in liver, spleen, and bone marrow | Part of hemoglobin molecule; catalyzes vitamin A formation; incorporated into a number of enzymes | Liver, lean meats, dried apricots, raisins, enriched whole-grain cereals, legumes, molasses; RDA = 10–18 mg |
| Manganese (Mn) | Most concentrated in liver, kidneys, and pancreas | Activates enzymes required for fatty acids and cholesterol synthesis, urea formation, and normal functioning of the nervous system | Nuts, legumes, whole-grain cereals, leafy green vegetables, fruits; RDA = 2.5–5 mg |
| Copper (Cu) | Most highly concentrated in liver, heart, and brain | Essential for hemoglobin synthesis, bone development, melanin production, and myelin formation | Liver, oysters, crabmeat, nuts, whole-grain cereals, legumes; RDA = 2–3 mg |
| Iodine (I) | Concentrated in thyroid gland | Essential component for synthesis of thyroid hormones | Food content varies with soil content in different geographic regions; iodized table salt; RDA = 0.15 mg |
| Cobalt (Co) | Widely distributed | Component of cyanocobalamin; required for synthesis of several enzymes | Liver, lean meats, milk; No RDA established |
| Zinc (Zn) | Most concentrated in liver, kidneys, and brain | Component of enzymes involved in digestion, respiration, bone metabolism, liver metabolism; necessary for normal wound healing and maintaining skin integrity | Meats, cereals, legumes, nuts, vegetables; RDA = 15 mg |
| Fluorine (F) | Primarily in bones and teeth | Component of tooth structure (enamel) | Fluoridated water; RDA = 1.5–4.0 mg |
| Selenium (Se) | Concentrated in liver and kidneys | Component of certain enzymes | Lean meats, fish, cereals; RDA = 0.05–2.00 mg |
| Chromium (Cr) | Widely distributed | Essential for use of carbohydrates | Liver, lean meats, wine; RDA = 0.05–2.00 mg |

*RDA = recommended daily allowance.

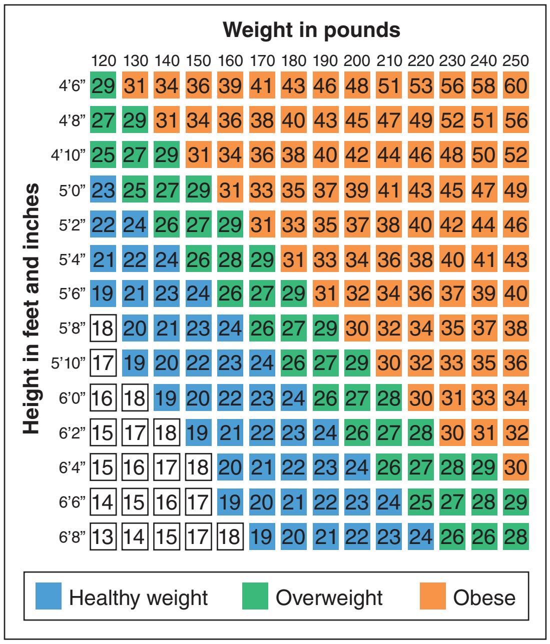
**Malnutrition** (mal″nu-trish′un) is poor nutrition that results from a lack of essential nutrients or an inability to utilize them. It may result from *undernutrition* and produce the symptoms of deficiency diseases, or it may be due to *overnutrition* arising from excess nutrient intake.

A variety of factors can lead to malnutrition. For example, a deficiency condition may stem from lack of availability or the poor quality of food. On the other hand, malnutrition may result from overeating or from taking too many vitamin supplements.

A measurement called the *body mass index* (BMI) is used to determine whether a person is of adequate weight, overweight, or obese. To calculate your BMI, divide your weight in kilograms (a kilogram equals 2.2 pounds) by your height in meters squared (one foot equals about .3 meters). Figure 15.34 interprets the BMI. Clinical Application 15.4 discusses the effects of undereating and overeating.

## PRACTICE

71. What is an adequate diet?
72. Which factors influence individual nutrient requirements?
73. What causes malnutrition?



| | 120 | 130 | 140 | 150 | 160 | 170 | 180 | 190 | 200 | 210 | 220 | 230 | 240 | 250 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 4′6″ | 🟩 29 | 🟧 31 | 🟧 34 | 🟧 36 | 🟧 39 | 🟧 41 | 🟧 43 | 🟧 46 | 🟧 48 | 🟧 51 | 🟧 53 | 🟧 56 | 🟧 58 | 🟧 60 |
| 4′8″ | 🟩 27 | 🟩 29 | 🟧 31 | 🟧 34 | 🟧 36 | 🟧 38 | 🟧 40 | 🟧 43 | 🟧 45 | 🟧 47 | 🟧 49 | 🟧 52 | 🟧 51 | 🟧 56 |
| 4′10″ | 🟩 25 | 🟩 27 | 🟩 29 | 🟧 31 | 🟧 34 | 🟧 36 | 🟧 38 | 🟧 40 | 🟧 42 | 🟧 44 | 🟧 46 | 🟧 48 | 🟧 50 | 🟧 52 |
| 5′0″ | 🟦 23 | 🟩 25 | 🟩 27 | 🟩 29 | 🟧 31 | 🟧 33 | 🟧 35 | 🟧 37 | 🟧 39 | 🟧 41 | 🟧 43 | 🟧 45 | 🟧 47 | 🟧 49 |
| 5′2″ | 🟦 22 | 🟦 24 | 🟩 26 | 🟩 27 | 🟩 29 | 🟧 31 | 🟧 33 | 🟧 35 | 🟧 37 | 🟧 38 | 🟧 40 | 🟧 42 | 🟧 44 | 🟧 46 |
| 5′4″ | 🟦 21 | 🟦 22 | 🟦 24 | 🟩 26 | 🟩 28 | 🟩 29 | 🟧 31 | 🟧 33 | 🟧 34 | 🟧 36 | 🟧 38 | 🟧 40 | 🟧 41 | 🟧 43 |
| 5′6″ | 🟦 19 | 🟦 21 | 🟦 23 | 🟦 24 | 🟩 26 | 🟩 27 | 🟩 29 | 🟧 31 | 🟧 32 | 🟧 34 | 🟧 36 | 🟧 37 | 🟧 39 | 🟧 40 |
| 5′8″ | ☐ 18 | 🟦 20 | 🟦 21 | 🟦 23 | 🟦 24 | 🟩 26 | 🟩 27 | 🟩 29 | 🟧 30 | 🟧 32 | 🟧 34 | 🟧 35 | 🟧 37 | 🟧 38 |
| 5′10″ | ☐ 17 | 🟦 19 | 🟦 20 | 🟦 22 | 🟦 23 | 🟦 24 | 🟩 26 | 🟩 27 | 🟩 29 | 🟧 30 | 🟧 32 | 🟧 33 | 🟧 35 | 🟧 36 |
| 6′0″ | ☐ 16 | ☐ 18 | 🟦 19 | 🟦 20 | 🟦 22 | 🟦 23 | 🟦 24 | 🟩 26 | 🟩 27 | 🟩 28 | 🟧 30 | 🟧 31 | 🟧 33 | 🟧 34 |
| 6′2″ | ☐ 15 | ☐ 17 | ☐ 18 | 🟦 19 | 🟦 21 | 🟦 22 | 🟦 23 | 🟦 24 | 🟩 26 | 🟩 27 | 🟩 28 | 🟧 30 | 🟧 31 | 🟧 32 |
| 6′4″ | ☐ 15 | ☐ 16 | ☐ 17 | ☐ 18 | 🟦 20 | 🟦 21 | 🟦 22 | 🟦 23 | 🟦 24 | 🟩 26 | 🟩 27 | 🟩 28 | 🟩 29 | 🟧 30 |
| 6′6″ | ☐ 14 | ☐ 15 | ☐ 16 | ☐ 17 | 🟦 19 | 🟦 20 | 🟦 21 | 🟦 22 | 🟦 23 | 🟦 24 | 🟩 25 | 🟩 27 | 🟩 28 | 🟩 29 |
| 6′8″ | ☐ 13 | ☐ 14 | ☐ 15 | ☐ 17 | ☐ 18 | 🟦 19 | 🟦 20 | 🟦 21 | 🟦 22 | 🟦 23 | 🟦 24 | 🟩 26 | 🟩 26 | 🟩 28 |

🟦 Healthy weight 🟩 Overweight 🟧 Obese

Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion

**FIGURE 15.34** BMI can be calculated as weight/height$^2$. In this chart the calculations have been done. The uncolored squares indicate lower than healthy weight according to this index.

CLINICAL APPLICATION **15.4**

## Eating Extremes: Undereating and Overeating

It is difficult to determine a desirable body weight. The body mass index (BMI) is used to classify a person as underweight, normal weight, overweight, or obese.

Being thin is not a disease, but abnormal eating behavior may be. Anorexia nervosa is self-imposed starvation. The sufferer perceives herself or himself as overweight and eats barely enough to survive, losing as much as 25% of her or his body weight. Anorexia leads to low blood pressure, slowed or irregular heartbeat, constipation, and constantly feeling chilly. In the female, menstruation may stop as the body fat level plunges. Hair becomes brittle, the skin dries out, and soft, pale, fine body hair called *lanugo*, normally seen only on a fetus, grows to preserve body heat. A person with anorexia may be hospitalized so that intravenous feeding can prevent sudden death from heart failure due to an electrolyte imbalance. Psychotherapy and nutritional counseling may help identify and remedy the underlying cause of the abnormal eating behavior. Despite these interventions, 15–21% of people with anorexia die from the disease.

In bulimia, a person eats large amounts of food and then gets rid of the thousands of extra calories by vomiting, taking laxatives, or exercising frantically. The binge-and-purge cycle is very hard to break, even with psychotherapy and nutritional counseling.

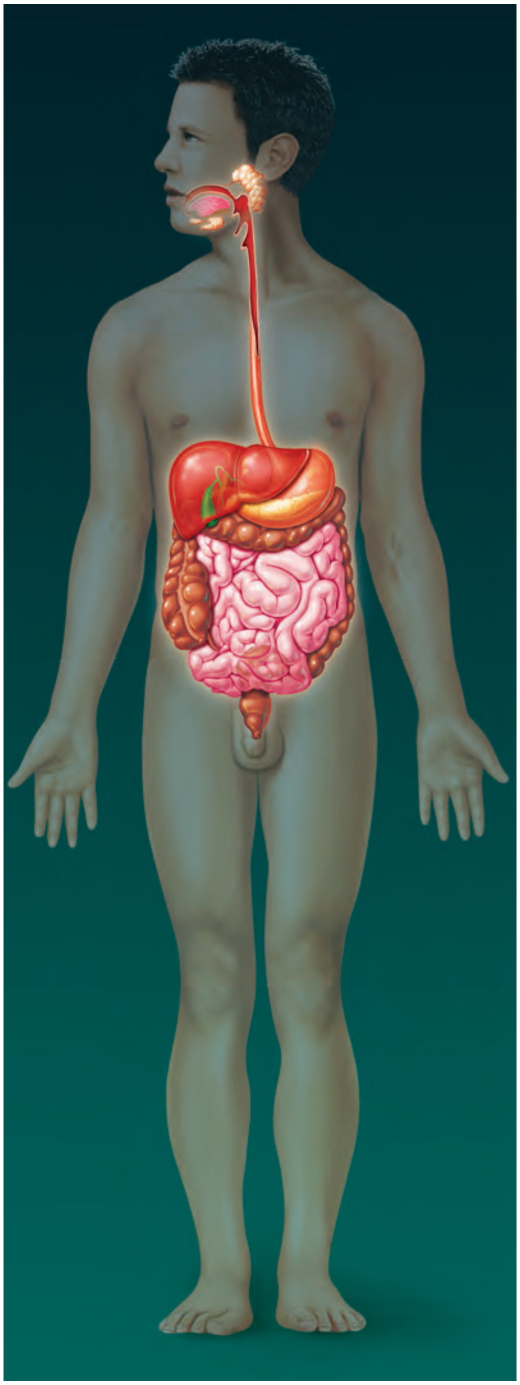
Because body weight reflects energy balance, excess food means, ultimately, excess weight. Being overweight or obese raises the risk of developing hypertension, diabetes, stroke, gallstones, sleep apnea, and certain cancers. The body strains to support the extra weight—miles of blood vessels are required to nourish additional body mass.

Usually, being overweight stems from overeating and inactivity. Weight loss requires eating less and exercising more. The National Heart, Lung, and Blood Institute recommends that overweight and obese individuals aim to lose 10 percent of their body weight over a 6-month period. For people with BMIs from 27 to 35, that means a decrease of 300 to 500 calories per day, to lose one-half to one pound of body weight per week. For people with BMIs exceeding 35, a decrease of up to 500 to 1,000 calories per day will translate to a loss of one to two pounds of body weight per week.

For people with BMIs above 40, or above 35 in addition to an obesity-related disorder, bariatric surgery can lead to great weight loss. Three types of procedures are done. In laparoscopic adjustable gastric banding, a silicone band ties off part of the stomach, limiting its capacity to hold food. The band can be inflated or deflated in a doctor's office by adding or removing saline. The band may need to be removed if it slips out of place, erodes the stomach lining, the body rejects it, or the port to add or remove fluid becomes displaced. In the second type of bariatric surgery, sleeve gastrectomy, a surgeon removes about 75% of the stomach, leaving a banana-shaped "sleeve." The sleeve procedure is irreversible. The third type of bariatric surgery is gastric bypass, in which part of the stomach is stapled shut, forming a pouch that is surgically connected to the jejunum, bypassing the duodenum.

All bariatric surgeries lead to decreased hunger, very reduced food intake, and some decrease in the absorption of nutrients. A special diet, liquid at first, must be followed. Many patients who have had bariatric surgery report improvement in or disappearance of type 2 diabetes, back pain, arthritis, varicose veins, sleep apnea, and hypertension. However, people can regain the weight and lose the benefits if they fail to adhere to the dietary restrictions.

# Digestive System

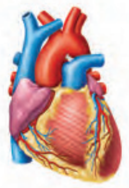


The digestive system ingests, digests, and absorbs nutrients for use by all body cells.

## Integumentary System

Vitamin D activated in the skin plays a role in absorption of calcium from the digestive tract.

## Cardiovascular System



The bloodstream carries absorbed nutrients to all body cells.

## Skeletal System

Bones are important in mastication. Calcium absorption is necessary to maintain bone matrix.

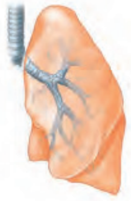
## Lymphatic System

The lymphatic system plays a major role in the absorption of fats.

## Muscular System

Muscles are important in mastication, swallowing, and the mixing and moving of digestion products through the gastrointestinal tract.

## Respiratory System



The digestive system and the respiratory system share anatomical structures.

## Nervous System

The nervous system can influence digestive system activity.

## Urinary System

The kidneys and liver work together to activate vitamin D.

## Endocrine System

Hormones can influence digestive system activity.

## Reproductive System

In a woman, nutrition is essential for conception and normal development of an embryo and fetus.

## Summary Outline

### 15.1 Introduction (p. 411)

*Digestion mechanically and chemically breaks down foods and absorbs the products. The digestive system consists of an alimentary canal and several accessory organs.*

### 15.2 General Characteristics of the Alimentary Canal (p. 411)

*The alimentary canal is a muscular tube.*

1. Structure of the wall
   The wall consists of four layers—the mucosa, submucosa, muscular layer, and serosa.
2. Movements of the tube
   Motor functions include mixing and propelling movements.

### 15.3 Mouth (p. 413)

*The mouth receives food and begins digestion.*

1. Cheeks and lips
   a. Cheeks consist of outer layers of skin, pads of fat, muscles associated with expression and chewing, and inner linings of epithelium.
   b. Lips are highly mobile and have sensory receptors.
2. Tongue
   a. The tongue's rough surface handles food and has taste buds.
   b. Lingual tonsils are on the root of the tongue.
3. Palate
   a. The palate includes hard and soft portions.
   b. Palatine tonsils are located on either side of the tongue in the back of the mouth.
4. Teeth
   a. There are twenty primary and thirty-two secondary teeth.
   b. Teeth begin mechanical digestion by breaking food into smaller pieces, increasing the surface area exposed to digestive actions.
   c. Each tooth consists of a crown and root, and is composed of enamel, dentin, pulp, nerves, and blood vessels.
   d. A periodontal ligament attaches a tooth to the alveolar process.

### 15.4 Salivary Glands (p. 418)

*Salivary glands secrete saliva, which moistens food, helps bind food particles, begins chemical digestion of carbohydrates, makes taste possible, and helps cleanse the mouth.*

1. Salivary secretions
   Salivary glands include serous cells that secrete digestive enzymes and mucous cells that secrete mucus.
2. Major salivary glands
   a. The parotid glands secrete saliva rich in amylase.
   b. The submandibular glands produce viscous saliva.
   c. The sublingual glands primarily secrete mucus.

### 15.5 Pharynx and Esophagus (p. 418)

*The pharynx and esophagus are important passageways.*

1. Structure of the pharynx
   The pharynx is divided into a nasopharynx, oropharynx, and laryngopharynx.
2. Swallowing mechanism
   Swallowing occurs in three stages:
   a. Food is mixed with saliva and forced into the oropharynx.
   b. Involuntary reflex actions move the food into the esophagus.
   c. Peristalsis transports food to the stomach.
3. Esophagus
   a. The esophagus passes through the diaphragm and joins the stomach.
   b. Circular muscle fibers at the distal end of the esophagus help prevent regurgitation of food from the stomach.

### 15.6 Stomach (p. 420)

*The stomach receives food, mixes it with gastric juice, carries on a limited amount of absorption, and moves food into the small intestine.*

1. Parts of the stomach
   a. The stomach is divided into cardia, fundus, body, and pylorus.
   b. The pyloric sphincter is a valve between the stomach and small intestine.
2. Gastric secretions
   a. Gastric glands secrete gastric juice.
   b. Gastric juice contains pepsin (begins chemical digestion of proteins), hydrochloric acid, and intrinsic factor.
3. Regulation of gastric secretions
   a. Parasympathetic impulses and the hormone gastrin enhance gastric secretion.
   b. Food in the small intestine reflexly inhibits gastric secretions.
4. Gastric absorption
   The stomach wall may absorb a few substances, such as water and other small molecules.
5. Mixing and emptying actions
   a. Mixing movements help produce chyme. Peristaltic waves move chyme into the pylorus.
   b. The muscular wall of the pylorus regulates chyme movement into the small intestine.
   c. The rate of emptying depends on the fluidity of chyme and the type of food present.

### 15.7 Pancreas (p. 423)

1. Structure of the pancreas
   a. The pancreas produces pancreatic juice that is secreted into a pancreatic duct.
   b. The pancreatic duct leads to the duodenum.
2. Pancreatic juice
   a. Pancreatic juice contains enzymes that can split carbohydrates, fats, nucleic acids, and proteins.
   b. Pancreatic juice has a high bicarbonate ion concentration that helps neutralize chyme and causes intestinal contents to be alkaline.
3. Hormones regulate pancreatic secretion
   a. Secretin stimulates the release of pancreatic juice with a high bicarbonate ion concentration.
   b. Cholecystokinin stimulates the release of pancreatic juice with a high concentration of digestive enzymes.

### 15.8 Liver (p. 424)

1. Liver structure
   a. The lobes of the liver consist of hepatic lobules, the functional units of the organ.
   b. Bile canals carry bile from hepatic lobules to hepatic ducts.
2. Liver functions
   a. The liver metabolizes carbohydrates, lipids, and proteins; stores some substances; filters blood; destroys toxins; and secretes bile.
   b. Bile is the only liver secretion that directly affects digestion.
3. Composition of bile
   a. Bile contains bile salts, bile pigments, cholesterol, and electrolytes.
   b. Only the bile salts have digestive functions.
4. Gallbladder
   a. The gallbladder stores bile between meals.
   b. A sphincter muscle controls release of bile from the bile duct.

5. Regulation of bile release
    a. Cholecystokinin from the small intestine stimulates bile release.
    b. The sphincter muscle at the base of the bile duct relaxes as a peristaltic wave in the duodenal wall approaches.
6. Functions of bile salts
    Bile salts emulsify fats and aid in the absorption of fatty acids, cholesterol, and certain vitamins.

### 15.9 Small Intestine (p. 430)

*The small intestine receives chyme from the stomach and secretions from the pancreas and liver, completes nutrient digestion, absorbs the products of digestion, and transports the residues to the large intestine.*

1. Parts of the small intestine
    The small intestine consists of the duodenum, jejunum, and ileum.
2. Structure of the small intestinal wall
    a. The wall is lined with villi that greatly increase the surface area and aid in mixing and absorption.
    b. Intestinal glands are located between the villi.
3. Secretions of the small intestine
    a. Secretions include mucus and digestive enzymes.
    b. Digestive enzymes embedded in the surfaces of microvilli split molecules of sugars, proteins, and fats into simpler forms.
4. Regulation of small intestine secretions
    Secretion is stimulated by chyme and parasympathetic reflexes stimulated by distension of the small intestinal wall.
5. Absorption in the small intestine
    a. Blood capillaries in the villi absorb monosaccharides and amino acids.
    b. Blood capillaries in the villi also absorb water and electrolytes.
    c. Fat molecules with longer chains of carbon atoms enter the lacteals of the villi.
    d. Fatty acids with relatively short carbon chains enter blood capillaries of the villi.
6. Movements of the small intestine
    a. Movements include mixing by segmentation and peristalsis.
    b. The ileocecal sphincter controls movement of the intestinal contents from the small intestine into the large intestine.

### 15.10 Large Intestine (p. 434)

*The large intestine reabsorbs water and electrolytes, and forms and stores feces.*

1. Parts of the large intestine
    a. The large intestine consists of the cecum, colon, rectum, and anal canal.
    b. The colon is divided into ascending, transverse, descending, and sigmoid portions.
2. Structure of the large intestinal wall
    a. The large intestinal wall resembles the wall in other parts of the alimentary canal.
    b. The large intestinal wall has a unique layer of longitudinal muscle fibers arranged in distinct bands.
3. Functions of the large intestine
    a. The large intestine has little or no digestive function.
    b. It secretes mucus.
    c. The large intestine absorbs water and electrolytes.
    d. The large intestine forms and stores feces.
4. Movements of the large intestine
    a. Movements are similar to those in the small intestine.
    b. Mass movements occur two to three times each day.
    c. A reflex stimulates defecation.
5. Feces
    a. Feces consist of water, undigested material, electrolytes, mucus, shed intestinal cells, and bacteria.
    b. The color of feces is due to bile pigments that have been altered by bacterial actions.

### 15.11 Nutrition and Nutrients (p. 438)

*Nutrition is the study of nutrients and how the body utilizes them. The macronutrients (carbohydrates, lipids, and proteins) are required in large amounts. The micronutrients (vitamins and minerals) are required in smaller amounts. Calories measure potential energy in foods.*

1. Carbohydrates
    a. Carbohydrate sources
        (1) Starch, glycogen, disaccharides, and monosaccharides are carbohydrates.
        (2) Cellulose is a polysaccharide that human enzymes cannot digest.
    b. Carbohydrate use
        (1) Oxidation releases energy from glucose.
        (2) Excess glucose is stored as glycogen or combined to produce fat.
        (3) Carbohydrates supply energy and are also part of nucleic acids and milk.
    c. Carbohydrate requirements
        (1) Humans survive with a wide range of carbohydrate intakes.
        (2) Excess carbohydrates may lead to weight gain.
2. Lipids
    a. Lipid sources
        (1) Foods of plant and animal origin provide triglycerides.
        (2) Foods of animal origin provide dietary cholesterol.
    b. Lipid use
        (1) The liver and adipose tissue control triglyceride metabolism.
        (2) Linoleic acid and linolenic acid are essential fatty acids.
        (3) Lipids supply energy and are used to build cell and organelle membranes and steroid hormones.
    c. Lipid requirements
        (1) The amounts and types of lipids needed for health are unknown.
        (2) Fat intake must be sufficient to carry fat-soluble vitamins.
3. Proteins
    a. Protein sources
        (1) Proteins are mainly obtained from meats, dairy products, cereals, and legumes.
        (2) Complete proteins contain adequate amounts of all the essential amino acids.
        (3) Incomplete proteins lack adequate amounts of one or more essential amino acids.
    b. Protein use
        Proteins serve as structural materials, function as enzymes, and provide energy.
    c. Protein requirements
        Proteins and amino acids must supply essential amino acids and nitrogen for the synthesis of nitrogen-containing molecules.

4. Vitamins
   a. Fat-soluble vitamins
      (1) These include vitamins A, D, E, and K.
      (2) They are carried in lipids and are influenced by the same factors that affect lipid absorption.
      (3) They resist the effects of heat; thus, they are not destroyed by cooking or food processing.
   b. Water-soluble vitamins
      (1) This group includes the B vitamins and vitamin C.
      (2) B vitamins make up a group (the vitamin B complex) and oxidize carbohydrates, lipids, and proteins.
      (3) Cooking or processing food destroys some water-soluble vitamins.
5. Minerals
   a. Characteristics of minerals
      (1) Most minerals are in the bones and teeth.
      (2) Minerals are usually incorporated into organic molecules; some occur in inorganic compounds or as free ions.
      (3) They serve as structural materials, function in enzymes, and play vital roles in metabolism.
   b. Major minerals include calcium, phosphorus, potassium, sulfur, sodium, chlorine, and magnesium.
   c. Trace elements include iron, manganese, copper, iodine, cobalt, zinc, fluorine, selenium, and chromium.
6. Adequate diets
   a. An adequate diet provides sufficient energy and essential nutrients to support optimal growth, maintenance, and repair of tissues.
   b. Individual requirements vary so greatly that designing a diet that is adequate for everyone is not possible. My Plate can help to personalize diets.
   c. Malnutrition may result from undernutrition or overnutrition.

## CHAPTER ASSESSMENTS

### 15.1 Introduction

**1.** Functions of the digestive system include ______. (p. 411)
   a. mechanical breakdown of foods
   b. chemical breakdown of foods
   c. breaking large pieces into smaller ones without altering their chemical composition
   d. all of the above

**2.** List the major parts of the alimentary canal, then separately list the accessory organs of the digestive system. (p. 411)

### 15.2 General Characteristics of the Alimentary Canal

**3.** Contrast the composition of the layers of the wall of the alimentary canal. (pp. 412–413)

**4.** Distinguish between mixing and propelling movements. (p. 413)

### 15.3 Mouth

**5.** Discuss the functions of the mouth and its parts. (p. 413)

**6.** Distinguish between primary and secondary teeth. (p. 416)

**7.** The teeth that are best adapted for grasping and tearing food are the ________. (p. 417)
   a. incisors
   b. canines
   c. premolars
   d. molars

**8.** Describe the structure of a tooth. (p. 417)

### 15.4–15.10 Salivary Glands–Large Intestine

**9.** Match the organ or gland with the enzyme(s) it secretes. Enzymes may be used more than once. An organ or gland may secrete more than one enzyme. (pp. 418–432)
   (1) salivary glands (serous cells)
   (2) stomach (chief cells)
   (3) pancreas (acinar cells)
   (4) small intestine (mucosal cells)

   A. peptidase
   B. amylase
   C. nuclease
   D. lipase
   E. pepsin
   F. trypsin, chymotrypsin, carboxypeptidase
   G. sucrase, maltase, lactase

**10.** Match the enzyme(s) with its (their) function(s). (pp. 418–432)
   (1) peptidase
   (2) amylase
   (3) nuclease
   (4) lipase
   (5) pepsin
   (6) trypsin, chymotrypsin, carboxypeptidase
   (7) sucrase, maltase, lactase

   A. begins protein digestion
   B. breaks fats into fatty acids and glycerol
   C. breaks down proteins into peptides
   D. breaks down starch into disaccharides
   E. breaks down peptides into amino acids
   F. breaks down nucleic acids into nucleotides
   G. breaks down disaccharides into monosaccharides

**11.** List the steps in swallowing. (p. 419)

**12.** Explain the stimulus for and response of the parasympathetic nervous system in digestion. (p. 422)

**13.** Explain how hormones control the secretions and/or release of secretions from the stomach, pancreas, and gallbladder. (pp. 422, 424, 428)

**14.** Discuss absorption of amino acids, monosaccharides, glycerol, fatty acids, electrolytes, and water from substances in the small and large intestines. (pp. 432–434 and 437)

**15.** List the steps in defecating. (p. 437)

### 15.11 Nutrition and Nutrients

**16.** Identify dietary sources of carbohydrates, lipids, and proteins. (pp. 438–441)

**17.** Explain how cells use carbohydrates, lipids, and proteins for the normal functioning of the body. (pp. 439–441)

**18.** Match the vitamins with their general functions, and indicate if the vitamin is fat-soluble or water-soluble. Functions may be used more than once, and more than one function may be applied to a vitamin. (pp. 442–443)

(1) vitamin A
(2) vitamin $B_1$ (thiamine)
(3) vitamin $B_2$ (riboflavin)
(4) vitamin $B_3$ (niacin)
(5) vitamin $B_5$ (pantothenic acid)
(6) vitamin $B_6$
(7) vitamin $B_7$ (biotin)
(8) vitamin $B_9$ (folacin)
(9) vitamin $B_{12}$ (cyanocobalamin)
(10) vitamin C (ascorbic acid)
(11) vitamin D
(12) vitamin E
(13) vitamin K

A. part of coenzyme A in oxidation of carbohydrates
B. required for ribose synthesis
C. necessary for synthesis of visual pigments
D. required for synthesis of prothrombin
E. required to produce collagen
F. required to synthesize nucleic acids
G. promotes red blood cell production
H. plays a role in myelin synthesis
I. antioxidant, helps stabilize cell membranes
J. promotes development of teeth and bones
K. required to produce antibodies
L. required for cellular growth
M. part of coenzymes to synthesize proteins, fats, and nucleic acids

**19.** Match the minerals/elements with their functions, and indicate whether each is a major mineral or a trace element required for nutrition. Functions may be used more than once, and more than one function may be applied to a mineral or trace element. (pp. 444 and 446)

(1) calcium
(2) chlorine
(3) chromium
(4) cobalt
(5) copper
(6) fluorine
(7) iodine
(8) iron
(9) magnesium
(10) manganese
(11) phosphorus
(12) potassium
(13) selenium
(14) sodium
(15) sulfur
(16) zinc

A. essential for the use of carbohydrates
B. component of certain enzymes
C. component of tooth enamel
D. component of teeth and bones
E. helps maintain intracellular osmotic pressure
F. essential part of certain amino acids
G. helps maintain extracellular fluid osmotic pressure
H. necessary for normal wound healing
I. component of cyanocobalamin
J. essential for synthesis of thyroid hormones
K. required in metabolic reactions associated with ATP production
L. component of hemoglobin molecules
M. essential for hemoglobin synthesis and melanin production
N. required for cholesterol synthesis and urea formation

**20.** Define *adequate diet*. (p. 444)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 11.9, 15.8, 15.11

**1.** Why does blood sugar concentration stay relatively stable in a person whose diet is low in carbohydrates?

### OUTCOMES 15.6, 15.11

**2.** How would removal of 95% of the stomach (subtotal gastrectomy) to treat severe ulcers or cancer affect digestion and absorption? How would the patient's eating habits have to be altered? Why? Do you think that people should have this type of surgery to treat life-threatening obesity?

### OUTCOMES 15.7, 15.8

**3.** Why might a person with inflammation of the gallbladder (cholecystitis) also develop inflammation of the pancreas (pancreatitis)?

### OUTCOME 15.11

**4.** Examine the label information on the packages of a variety of dry breakfast cereals. Which types of cereals provide adequate sources of vitamins and minerals? Which major nutrients are lacking in these cereals?

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**LearnSmart** Discover which chapter concepts you have mastered and which require more attention. This adaptive learning tool is personalized, proven, and preferred.

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# 16

# Respiratory System

*The danger of secondhand smoke, long debated, is now widely accepted, and new rules and regulations attempt to limit exposure.*

The dangers of secondhand smoke. Exposure to environmental tobacco smoke (ETS)—also called secondhand smoke—can be as dangerous as actually smoking. ETS has two sources: *sidestream smoke* from lit cigarettes, cigars, or pipes, and *mainstream smoke* that smokers exhale. Smoke contains more than 4,000 chemicals, many of which are irritants, carcinogens, mutagens, or systemic or developmental toxins. More than sixty carcinogens are in tobacco smoke. Toxins include benzene, formaldehyde, vinyl chloride, ammonia, arsenic, and cyanide.

Exposure to ETS likely kills an estimated 53,000 nonsmokers in the United States each year. That includes 46,000 heart disease deaths and 3,400 lung cancer deaths.

ETS is especially dangerous for children. It worsens asthma, increases susceptibility to ear infections, and is associated with low birth weight. ETS is also responsible for 150,000 to 300,000 cases of lower respiratory infection (bronchitis or pneumonia) in children under eighteen months of age.

Even short exposures to smoke are dangerous, to anyone. Just a half hour of breathing someone else's smoke can activate platelets, damage endothelium, and decrease coronary artery blood flow—all changes that set the stage for cardiovascular disease.

The only way to decrease exposure to ETS is to eliminate it. Dividing a space into smoking and nonsmoking areas does not work, because the smoke lingers for hours—this is why airplanes, many restaurants, and many workplaces are smoke-free. The *U.S. Surgeon General's Report on the Health Consequences of Involuntary Exposure to Tobacco Smoke* concluded that there is "no risk-free level of exposure to secondhand smoke."

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

### 16.1 Introduction

1. Identify the general functions of the respiratory system. (p. 454)

### 16.2 Organs and Associated Structures of the Respiratory System

2. Locate the organs and associated structures of the respiratory system. (pp. 454–460)
3. Describe the functions of each organ of the respiratory system. (pp. 454–460)

### 16.3 Breathing Mechanism

4. Explain the mechanisms of inspiration and expiration. (pp. 460–464)
5. Define each of the respiratory volumes and capacities. (pp. 465 and 467)

### 16.4 Control of Breathing

6. Locate the respiratory areas in the brainstem and explain how they control breathing. (p. 468)
7. Discuss how various factors affect the respiratory areas. (p. 469)

### 16.5 Alveolar Gas Exchanges

8. Describe the structure and function of the respiratory membrane. (p. 470)
9. Explain how air and blood exchange gases. (p. 471)

### 16.6 Gas Transport

10. List the ways blood transports oxygen and carbon dioxide. (pp. 472–474)

Anatomy & Physiology REVEALED aprevealed.com **Module 11** Respiratory System

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**alveol-** [small cavity] *alveol*us: Microscopic air sac within a lung.

**bronch-** [windpipe] *bronch*us: Branch of the trachea.

**cric-** [ring] *cric*oid cartilage: Ring-shaped mass of cartilage at the base of the larynx.

**epi-** [upon] *epi*glottis: Flaplike structure that partially covers the opening into the larynx during swallowing.

**hemo-** [blood] *hemo*globin: Pigment in red blood cells that transports oxygen and carbon dioxide.

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## 16.1 | Introduction

Cells require oxygen to break down nutrients to release energy and produce ATP, and must excrete the carbon dioxide that results. Obtaining oxygen and removing carbon dioxide are the primary functions of the **respiratory system.** It includes tubes that remove (filter) particles from incoming air and transport air into and out of the lungs, as well as microscopic air sacs where gases are exchanged. The respiratory system also entraps particles from incoming air, help control the temperature and water content of the air, produce vocal sounds, and participate in the sense of smell and the regulation of blood pH.

The entire process of gas exchange between the atmosphere and cells is called **respiration** (res″pĭ-ra′shun). The events of respiration include: (1) movement of air into and out of the lungs—commonly called breathing or *ventilation;* (2) gas exchange between the blood and the air in the lungs (external respiration); (3) gas transport in the blood between the lungs and body cells; and (4) gas exchange between the blood and the cells (internal respiration). The process of oxygen utilization and carbon dioxide production at the cellular level is called *cellular respiration.*

**PRACTICE**

1. What is respiration?

## 16.2 | Organs and Associated Structures of the Respiratory System

The respiratory system can be divided into two parts, or tracts. The *upper respiratory tract* includes the nose, nasal cavity, paranasal sinuses, and pharynx. The *lower respiratory tract* includes the larynx, trachea, bronchial tree, and lungs (fig. 16.1; see reference plates 3, 4, 5, and 6, pp. 34–37).

### Nose

Bone and cartilage support the **nose** internally. Its two *nostrils* are openings through which air can enter and leave the nasal cavity. Many internal hairs guard the nostrils, preventing entry of large particles carried in the air.

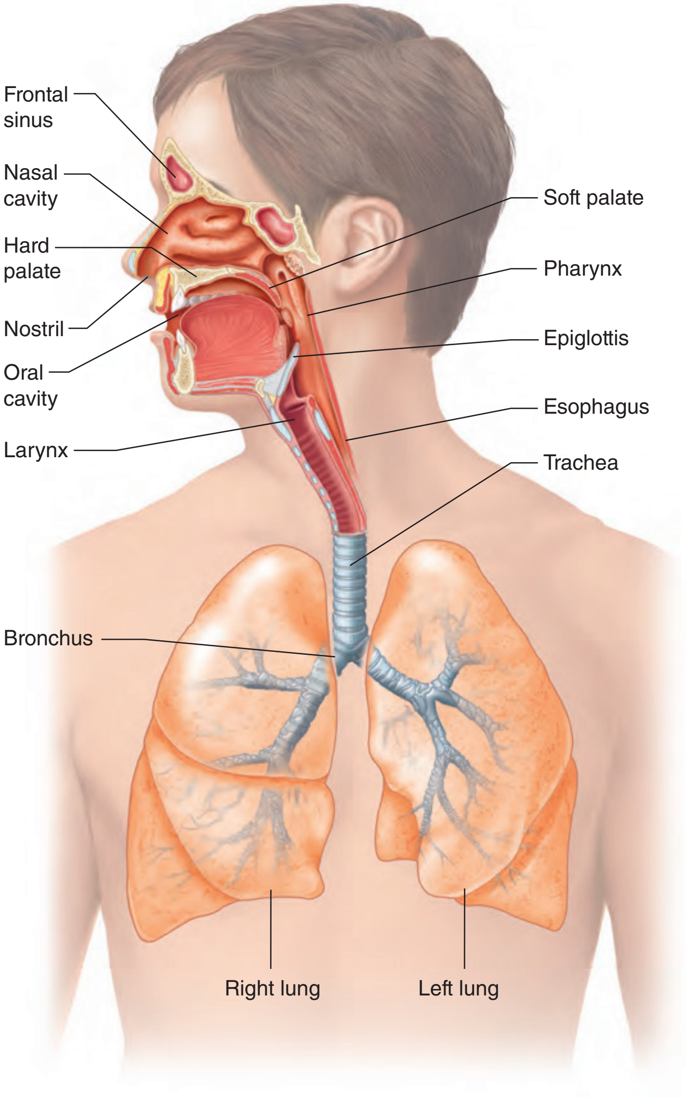


**FIGURE 16.1** Organs and associated structures of the respiratory system.

## Nasal Cavity

The **nasal cavity** is a hollow space behind the nose (fig. 16.1). The **nasal septum,** composed of bone and cartilage, divides the nasal cavity into right and left parts. **Nasal conchae** are bones and bone processes that curl out from the lateral walls of the nasal cavity on each side, dividing the cavity into passageways (fig. 16.2). Nasal conchae also support the mucous membrane that lines the nasal cavity and help increase its surface area.

The mucous membrane has pseudostratified ciliated epithelium that is rich in mucus-secreting goblet cells (see chapter 5, p. 108). It also includes an extensive network of blood vessels. As air passes over the mucous membrane, heat leaves the blood and warms the air, adjusting the air's temperature to that of the body. In addition, incoming air is moistened as water evaporates from the mucous lining. The sticky mucus that the mucous membrane secretes entraps dust and other small particles entering with the air.

The nasal septum is usually straight at birth, but it can bend as the result of a birth injury. With age, the septum bends toward one side or the other. If such a *deviated septum* is severe, it may obstruct the nasal cavity, making breathing difficult.

As the cilia of the epithelial lining move, they push a thin layer of mucus and entrapped particles toward the pharynx, where the mucus is swallowed (fig. 16.3). In the stomach, gastric juice destroys microorganisms in the mucus.

**FACTS OF LIFE** A spore of the bacterium that causes anthrax is only half a micrometer wide. When spores are combined with powder to create a "bioweapon," they are still small enough to bypass the hairs and mucus in the nose, reaching the lungs, where they can cause inhalation anthrax. The bacteria release a toxin that causes death.

## Paranasal Sinuses

Recall from chapter 7 (pp. 155–159) that the **paranasal sinuses** are air-filled spaces within the *frontal, ethmoid, sphenoid,* and *maxillary bones* of the skull that open into the nasal cavity. Mucous membranes line the sinuses and are continuous with the lining of the nasal cavity. The paranasal sinuses reduce the weight of the skull and are resonant chambers that affect the quality of the voice.

A painful sinus headache can result from blocked drainage caused by an infection or allergic reaction.

**PRACTICE**

2. Which organs constitute the respiratory system?
3. What are the functions of the mucous membrane that lines the nasal cavity?
4. Where are the paranasal sinuses?
5. What are the functions of the paranasal sinuses?

## Pharynx

The **pharynx,** or throat, is behind the oral cavity, the nasal cavity, and the larynx (see fig. 16.1). It is a passageway for food moving from the oral cavity to the esophagus and for air passing between the nasal cavity and the larynx. The pharynx also helps produce the sounds of speech. Chapter 15 (p. 419) describes the subdivisions of the pharynx—the nasopharynx, oropharynx, and laryngopharynx, which are shown in figure 16.2.

### CAREER CORNER

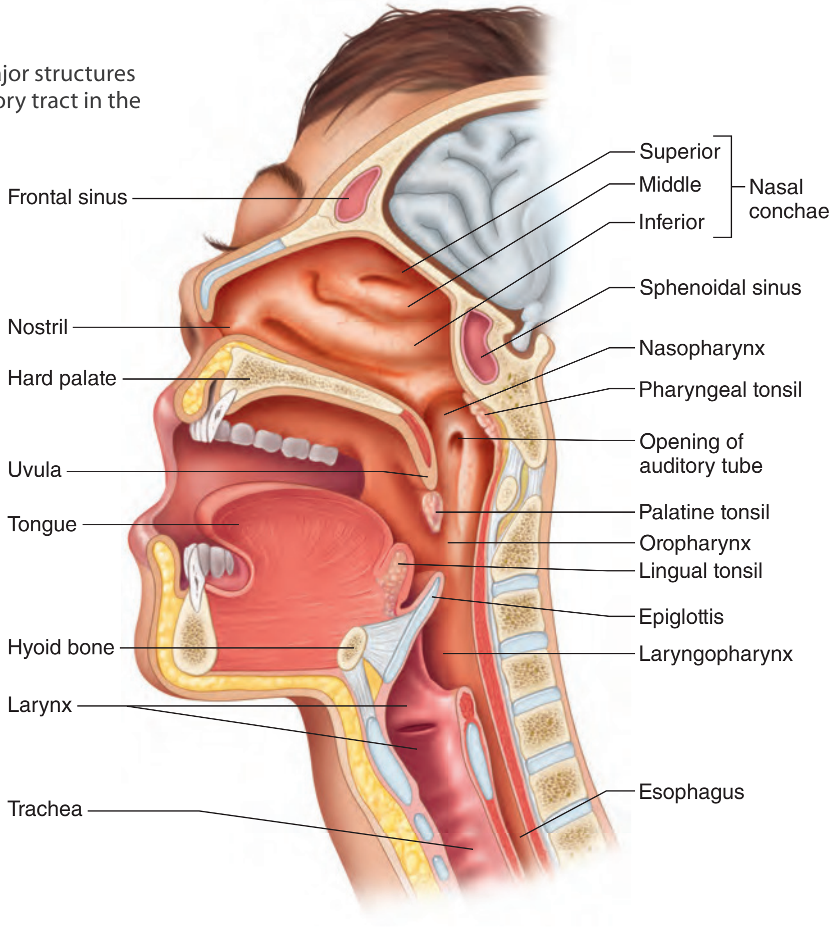
### Respiratory Therapist

The teachers welcome an education session from the local hospital's respiratory therapist, who has taken time away from her patient responsibilities to talk to the class. Several children in the elementary school have asthma, and the teachers have requested this education session so that they can better understand the condition. After the session, they feel more confident that they can help the students and also explain to their classmates what is happening.

Respiratory therapists assess patients who are experiencing breathing problems and treat them, under supervision of a physician. They work in diverse places and under a variety of situations. A respiratory therapist might help a patient breathe on his or her own following anesthesia, instruct a patient newly diagnosed with emphysema on how to use supplemental oxygen, check on how hospitalized patients are breathing, or teach parents of a young child with cystic fibrosis how to apply pressure to the chest to shake free the thick mucus that builds up. They assist patients in using specialized equipment, such as that used to treat sleep apnea or a home ventilator for a patient with a spinal cord injury. The overall goal is to help patients be as independent as possible.

A respiratory therapist applies knowledge of how the heart and lungs function. Educational requirements include at least an associate's degree and certification, plus continuing education.

**FIGURE 16.2** APIR Major structures associated with the respiratory tract in the head and neck.


Frontal sinus
Nostril
Hard palate
Uvula
Tongue
Hyoid bone
Larynx
Trachea
Superior
Middle
Inferior
Nasal conchae
Sphenoidal sinus
Nasopharynx
Pharyngeal tonsil
Opening of auditory tube
Palatine tonsil
Oropharynx
Lingual tonsil
Epiglottis
Laryngopharynx
Esophagus

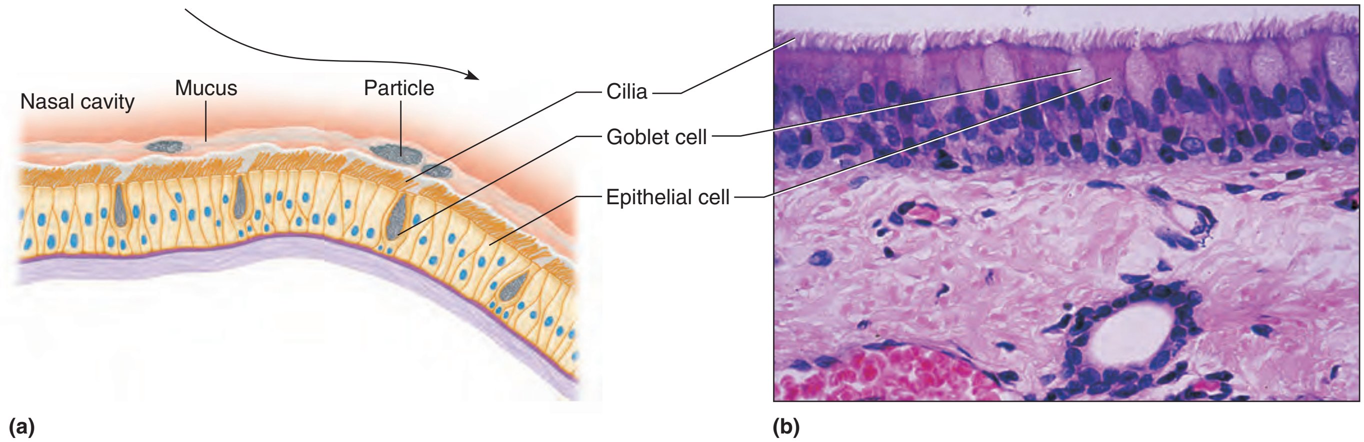

Nasal cavity
Mucus
Particle
Cilia
Goblet cell
Epithelial cell
(a)
(b)

**FIGURE 16.3** APIR Mucus movement in the respiratory tract. (**a**) Cilia move mucus and trapped particles from the nasal cavity to the pharynx. (**b**) Micrograph of ciliated epithelium in the respiratory tract (275×).

## Larynx

The **larynx** (lar′inks) is an enlargement in the airway at the top of the trachea and below the oropharynx. It conducts air in and out of the trachea and prevents foreign objects from entering the trachea. It also houses the *vocal cords.*

The larynx is composed of a framework of muscles and cartilages bound by elastic tissue. The largest of the cartilages are the *thyroid* ("Adam's apple"), *cricoid,* and *epiglottic cartilages* (fig. 16.4).

Inside the larynx, two pairs of horizontal *vocal folds* composed of muscle tissue and connective tissue with a covering of mucous membrane extend inward from the lateral walls. The upper folds are called *false vocal cords* because they do not produce sounds (fig. 16.5*a*). Muscle fibers within these folds help close the airway during swallowing.

The lower folds of muscle tissue and elastic fibers are the *true vocal cords.* Air forced between the true vocal cords causes them to vibrate from side to side,

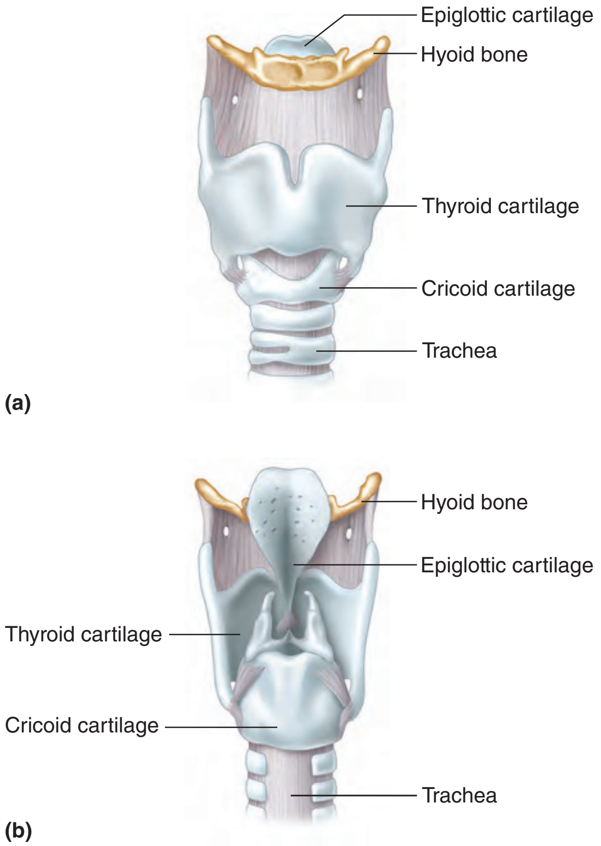

Epiglottic cartilage
Hyoid bone
Thyroid cartilage
Cricoid cartilage
Trachea
(a)
Hyoid bone
Epiglottic cartilage
Thyroid cartilage
Cricoid cartilage
Trachea
(b)

**FIGURE 16.4** APR Larynx. (**a**) Anterior and (**b**) posterior views of the larynx.

which generates sound waves. Changing the shapes of the pharynx and oral cavity and using the tongue and lips transform these sound waves into words.

Contracting or relaxing muscles that alter the tension on the vocal cords controls the pitch (musical tone) of a sound. Increasing tension raises pitch, and decreasing tension lowers pitch. The intensity (loudness) of a sound reflects the force of air passing through the vocal folds. Stronger blasts of air produce louder sound; weaker blasts produce softer sound.

Damage to the nerves (recurrent laryngeal nerves) that supply the laryngeal muscles can alter the quality of a person's voice. These nerves pass through the neck as parts of the vagus nerves, and trauma or surgery to the neck or thorax can injure them. Nodules or other growths on the margins of the vocal folds that interfere with the free flow of air can also cause vocal problems. Sometimes surgery may be necessary to remove such lesions.

During normal breathing, the vocal cords are relaxed and the opening between them, called the **glottis** (glot′is), is a triangular slit. When a person swallows food or liquid, muscles in the false vocal cords close the glottis, which prevents the material from entering the trachea (fig. 16.5).

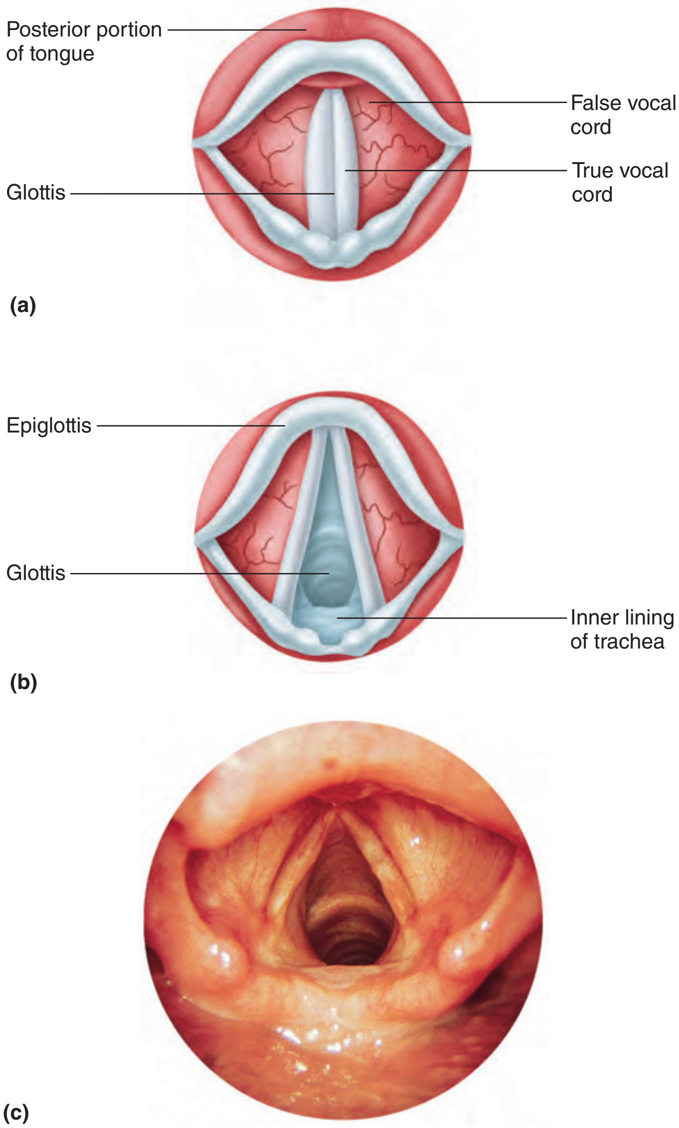

Posterior portion of tongue
False vocal cord
True vocal cord
Glottis
(a)
Epiglottis
Glottis
Inner lining of trachea
(b)
(c)

**FIGURE 16.5** The vocal cords as viewed from above with the glottis (**a**) closed and (**b**) open. (**c**) Photograph of the open glottis and vocal folds.

The epiglottic cartilage is the central part of a flaplike structure called the **epiglottis.** This structure usually stands upright and allows air to enter the larynx. During swallowing the larynx rises and the epiglottis presses downward, partially covering the opening into the larynx. This action helps prevent foods and liquids from entering the air passages (see chapter 15, p. 419).

*Laryngitis*—which causes hoarseness or lack of voice—occurs when the mucous membrane of the larynx becomes inflamed and swollen, due to an infection or an irritation from inhaled vapors, and prevents the vocal cords from vibrating freely. Laryngitis is usually mild, but may be dangerous if swollen tissues obstruct the airway and interfere with breathing. Inserting a tube (endotracheal tube) into the trachea through the mouth can restore the passageway until the inflammation subsides.

## PRACTICE

6. Describe the structure of the larynx.
7. How do the vocal cords produce sounds?
8. What is the function of the glottis? The epiglottis?

## Trachea

The **trachea** (tra′ke-ah), or windpipe, is a flexible cylindrical tube about 2.5 centimeters in diameter and 12.5 centimeters in length (fig. 16.6). It extends downward anterior to the esophagus and into the thoracic cavity, where it splits into right and left bronchi.

A ciliated mucous membrane with many goblet cells lines the trachea's inner wall. This membrane filters incoming air and moves entrapped particles upward into the pharynx, where the mucus can be swallowed. The Genetics Connection 16.1 entitled "Cystic Fibrosis" discusses what happens when the mucus formed is extremely thick.

Within the tracheal wall are about twenty C-shaped pieces of hyaline cartilage, one above the other. The open ends of these incomplete rings are directed posteriorly, and smooth muscle and connective tissues fill the gaps between the ends. These cartilaginous rings prevent the trachea from collapsing and blocking the airway. The soft tissues that complete the rings in the back allow the nearby esophagus to expand as food moves through it to the stomach.

## Bronchial Tree

The **bronchial tree** (brong′ke-al tre) consists of branched airways leading from the trachea to the microscopic air sacs in the lungs (fig. 16.7). Its branches begin with the right and left **main (primary) bronchi,** which arise from the trachea at the level of the fifth thoracic vertebra. Each bronchus enters its respective lung.

Each main bronchus divides into lobar (secondary) bronchi a short distance from its origin. The lobar bronchi branch into segmental (tertiary) bronchi, and then into increasingly finer tubes. Among these smaller tubes are **bronchioles** that continue to branch, giving rise to terminal bronchioles, respiratory bronchioles, and finally to very thin tubes called **alveolar ducts.** These ducts lead to thin-walled outpouchings called **alveolar sacs.** Alveolar sacs lead to smaller, microscopic air sacs called **alveoli** (al-ve′o-li; singular, alve-

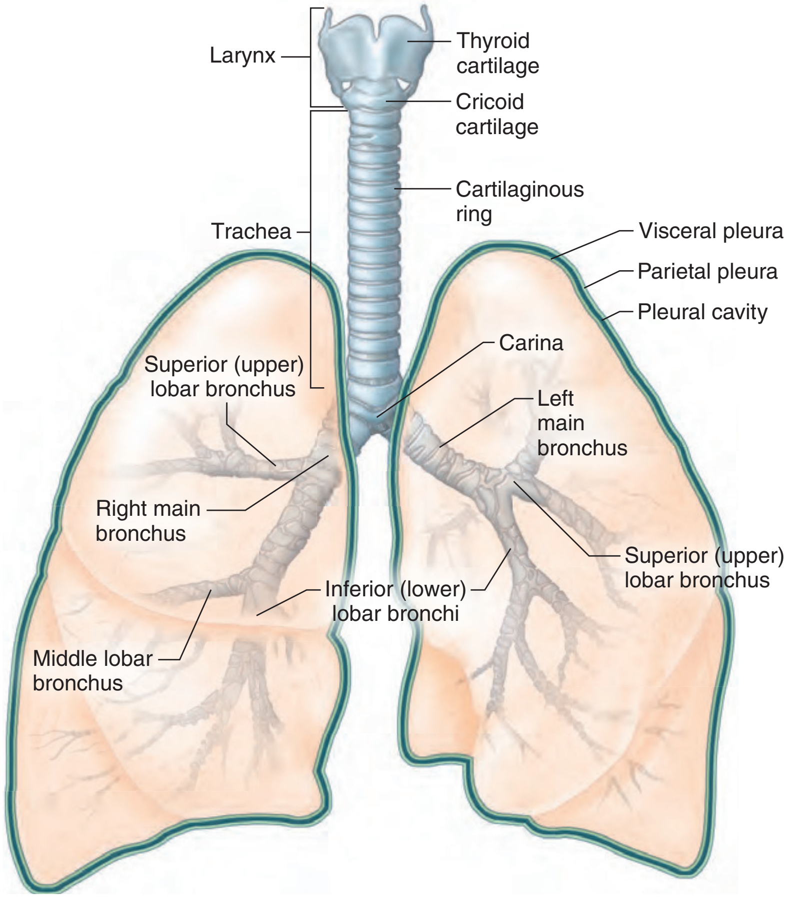

Larynx
Thyroid cartilage
Cricoid cartilage
Cartilaginous ring
Trachea
Visceral pleura
Parietal pleura
Pleural cavity
Carina
Superior (upper) lobar bronchus
Left main bronchus
Right main bronchus
Superior (upper) lobar bronchus
Inferior (lower) lobar bronchi
Middle lobar bronchus

**FIGURE 16.6** The trachea conducts air between the larynx and the bronchi.

## GENETICS CONNECTION 16.1

## Cystic Fibrosis

Young children who cannot pronounce the name of their disease call it "65 Roses." Cystic fibrosis (CF) is an inherited defect in ion channels that control chloride movement out of cells in certain organs. In the lungs, thick, sticky mucus accumulates and creates an environment hospitable to certain bacteria that are not common in healthy lungs. A mucus-clogged pancreas prevents digestive secretions from reaching the intestines, impairing nutrient digestion and absorption. A child with CF has trouble breathing and maintaining weight.

CF is inherited from two carrier parents, and affects about 30,000 people in the United States and about 70,000 worldwide. Many others may have milder cases, with recurrent respiratory infections. More than 1600 mutations have been recognized in the cystic fibrosis transmembrane receptor (*CFTR*) gene, which encodes the chloride channel protein. Today newborns with CF are diagnosed using a genetic test shortly after birth, but years ago the first signs were typically "failure to thrive," salty sweat, and foul-smelling stools.

When CF was recognized in 1938, life expectancy was only five years, but today median survival is about age forty, with many patients living longer, thanks to drug treatments. Inhaled antibiotics control the respiratory infections, and daily "bronchial drainage" exercises shake stifling mucus from the lungs. A vibrating vest worn for half-hour periods two to four times a day also loosens mucus. Digestive enzymes mixed into soft foods enhance nutrient absorption, although some patients require feeding tubes.

Discovery of the most common *CFTR* mutation in 1989 enabled development of more-targeted treatments. Thirty drugs are now in development. The new drugs work in various ways: correcting misfolded *CFTR* protein, restoring liquid on airway surfaces, breaking up mucus, improving nutrition, and fighting inflammation and infection.

Life with severe CF is challenging. In summertime, a child must avoid water from hoses, which harbor lung-loving *Pseudomonas* bacteria. Cookouts spew lung-irritating particulates. Too much chlorine in pools irritates lungs, whereas too little invites bacterial infection. New infections arise, too. In the past few years, multidrug-resistant *Mycobacterium abscessus*, related to the pathogen that causes tuberculosis, has affected 3% to 10% of CF patients in the United States and Europe.

olus), which lie within capillary networks (figs. 16.8 and 16.9).

The structure of a bronchus is similar to that of the trachea, but the tubes that branch from it have less cartilage in their walls, and the bronchioles lack cartilage. As the cartilage diminishes, a layer of smooth muscle surrounding the tube becomes more prominent. This muscular layer persists even in the smallest bronchioles, but only a few muscle fibers are in the alveolar ducts.

The branches of the bronchial tree are air passages whose mucous membranes filter incoming air and distribute the air to alveoli throughout the lungs. The alveoli provide a large surface area of thin simple squamous epithelial cells through which gases are easily exchanged. Oxygen diffuses from the alveoli into the blood in nearby capillaries, and carbon dioxide diffuses from the blood into the alveoli (fig. 16.10).

**FACTS OF LIFE** Combined, two adult lungs have about 300 million alveoli, providing a total surface area nearly half the size of a tennis court.

### PRACTICE

9. What is the function of the cartilaginous rings in the tracheal wall?
10. Describe the bronchial tree.
11. Predict the direction of diffusion of gases between alveoli and alveolar capillaries.

## Lungs

The **lungs** are soft, spongy, cone-shaped organs in the thoracic cavity (see fig. 16.1 and reference plates 4 and 5, pp. 35–36). The mediastinum separates the right and left lungs medially, and the diaphragm and thoracic cage enclose them.

Each lung occupies most of the thoracic space on its side. A bronchus and some large blood vessels suspend each lung in the cavity. These tubular structures enter the lung on its medial surface. A layer of serous membrane, the **visceral pleura** (vis′er-al ploo′rah), firmly attaches to each lung surface and folds back to become the **parietal pleura** (pah-ri′ĕ-tal ploo′rah). The parietal

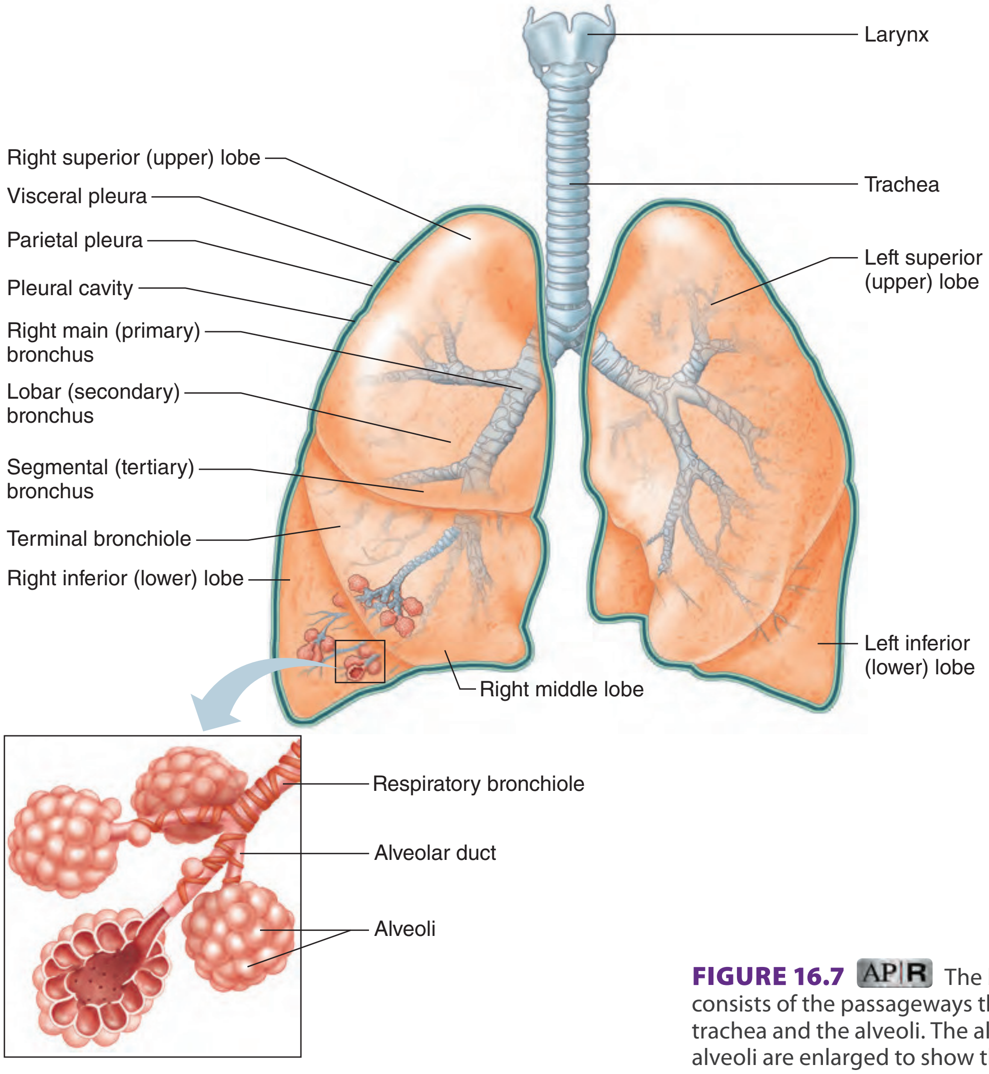

Larynx
Trachea
Right superior (upper) lobe
Visceral pleura
Parietal pleura
Pleural cavity
Right main (primary) bronchus
Lobar (secondary) bronchus
Segmental (tertiary) bronchus
Terminal bronchiole
Right inferior (lower) lobe
Left superior (upper) lobe
Left inferior (lower) lobe
Right middle lobe
Respiratory bronchiole
Alveolar duct
Alveoli

**FIGURE 16.7** APR The bronchial tree consists of the passageways that connect the trachea and the alveoli. The alveolar ducts and alveoli are enlarged to show their locations.

pleura, in turn, forms part of the mediastinum and lines the inner wall of the thoracic cavity (fig. 16.11).

No significant space exists between the visceral and parietal pleurae, but the potential space between them is called the **pleural cavity** (ploo′ral kav′ĭ-te). It has a thin film of serous fluid that lubricates adjacent pleural surfaces, reducing friction as they move against one another during breathing. This fluid also helps hold the pleural membranes together, as explained in section 16.3.

The right lung is larger than the left one and is divided into three lobes. The left lung has two lobes (see figs. 16.1 and 16.7).

A major branch of the bronchial tree supplies each lobe. A lobe also has connections to blood and lymphatic vessels and lies within connective tissues. Thus, a lung includes air passages, alveoli, blood vessels, connective tissues, lymphatic vessels, and nerves. Table 16.1 summarizes the characteristics of the major parts of the respiratory system.

**PRACTICE**

12. Where are the lungs located?
13. What is the function of serous fluid in the pleural cavity?
14. What types of structures make up a lung?

## 16.3 | Breathing Mechanism

Breathing, or ventilation, is the movement of air from outside the body first into and then out of the bronchial tree and alveoli. The actions providing these air movements are termed **inspiration** (in″spĭ-ra′shun), or inhalation, and **expiration** (ek″spĭ-ra′shun), or exhalation.

### Inspiration

*Atmospheric pressure,* the pressure of the air around us, provides the force that moves air into the lungs. At sea level, this pressure is sufficient to support a column of

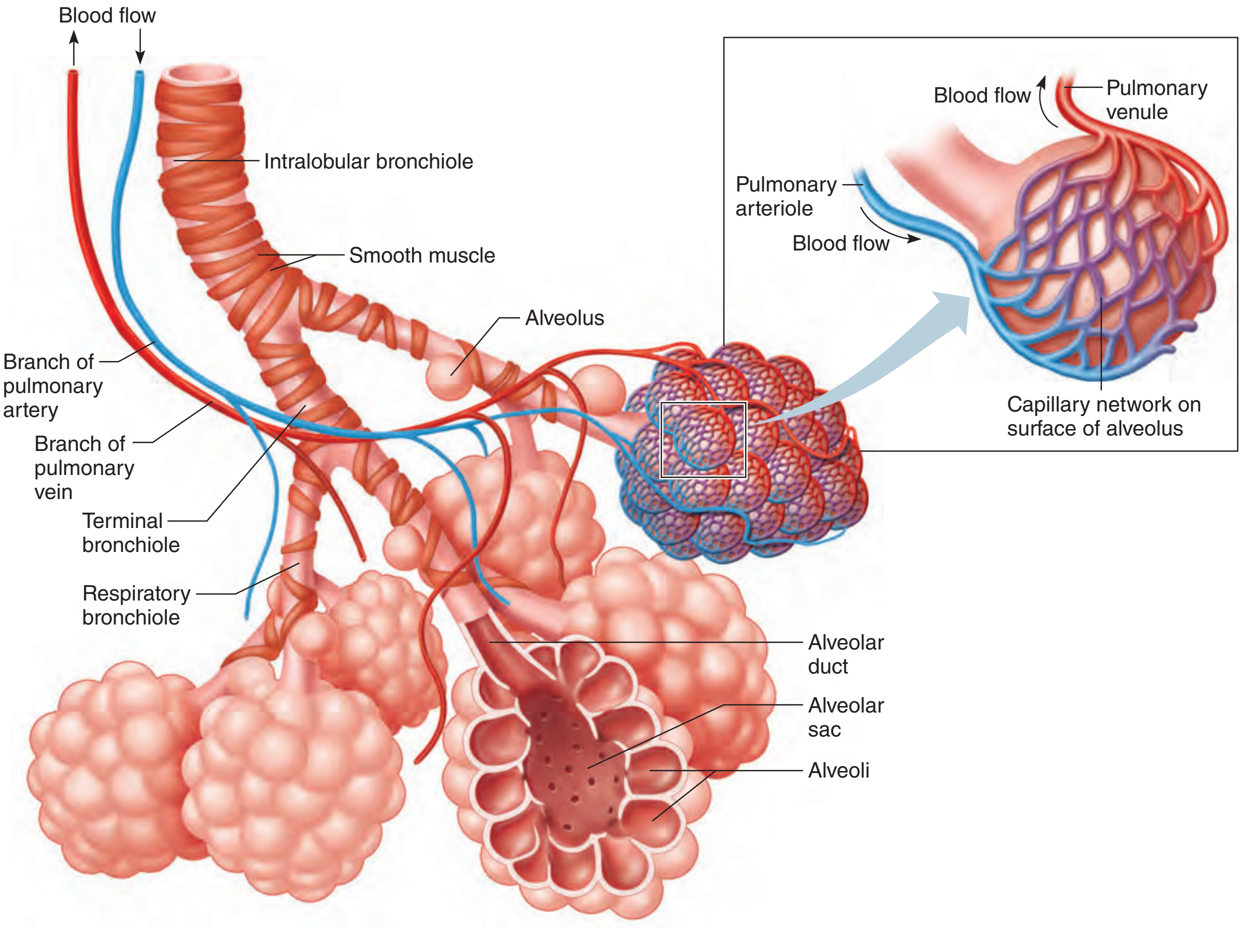

Blood flow
Intralobular bronchiole
Smooth muscle
Alveolus
Branch of pulmonary artery
Branch of pulmonary vein
Terminal bronchiole
Respiratory bronchiole
Alveolar duct
Alveolar sac
Alveoli
Blood flow
Pulmonary venule
Pulmonary arteriole
Blood flow
Capillary network on surface of alveolus

**FIGURE 16.8** APR The respiratory tubes end in tiny alveoli, each of which is surrounded by a capillary network.

Q *Why is the pulmonary artery colored blue in this figure?*
**Answer can be found in Appendix F on page 582.**

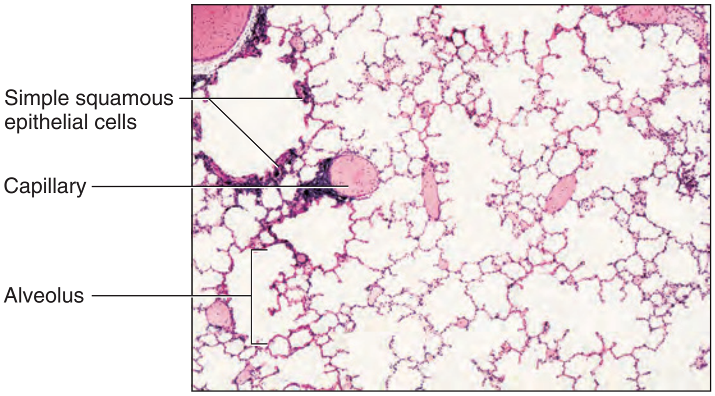

Simple squamous epithelial cells
Capillary
Alveolus

**FIGURE 16.9** APR Light micrograph of alveoli (250×).

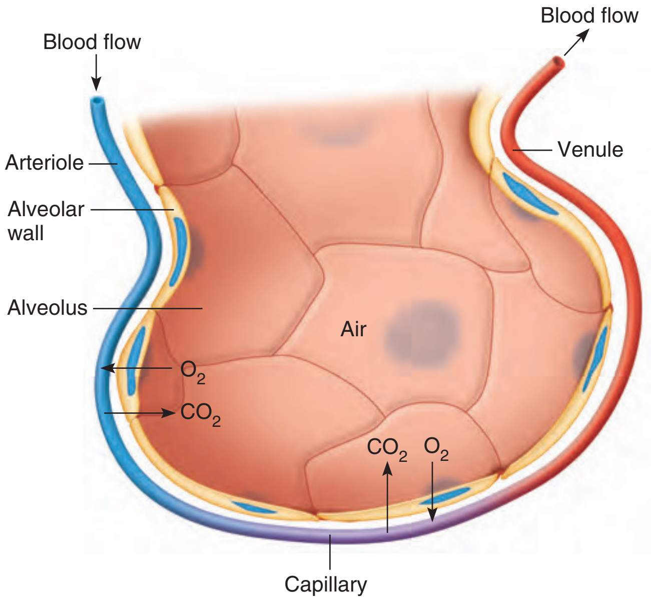

Blood flow
Blood flow
Arteriole
Venule
Alveolar wall
Alveolus
Air
$O_2$
$CO_2$
$CO_2$
$O_2$
Capillary

**FIGURE 16.10** APR Oxygen ($O_2$) diffuses from air within the alveolus into the capillary, while carbon dioxide ($CO_2$) diffuses from blood within the capillary into the alveolus.

**TABLE 16.1** Parts of the Respiratory System

| Part | Description | Function |
|---|---|---|
| Nose | Part of face centered above mouth, in and below space between eyes | Nostrils provide entrance to nasal cavity; internal hairs begin to filter incoming air |
| Nasal cavity | Hollow space behind nose | Conducts air to pharynx; mucous lining filters, warms, and moistens incoming air |
| Paranasal sinuses | Hollow spaces in certain skull bones | Reduce weight of skull; serve as resonant chambers |
| Pharynx | Chamber behind nasal cavity, oral cavity, and larynx | Passageway for air moving from nasal cavity to larynx and for food moving from oral cavity to esophagus |
| Larynx | Enlargement at top of trachea | Passageway for air; prevents foreign objects from entering trachea; houses vocal cords |
| Trachea | Flexible tube that connects larynx with bronchial tree | Passageway for air; mucous lining continues to filter particles from incoming air |
| Bronchial tree | Branched tubes that lead from trachea to alveoli | Conducts air from trachea to alveoli; mucous lining continues to filter incoming air |
| Lungs | Soft, cone-shaped organs that occupy a large portion of the thoracic cavity | Contain air passages, alveoli, blood vessels, connective tissues, lymphatic vessels, and nerves of the lower respiratory tract |

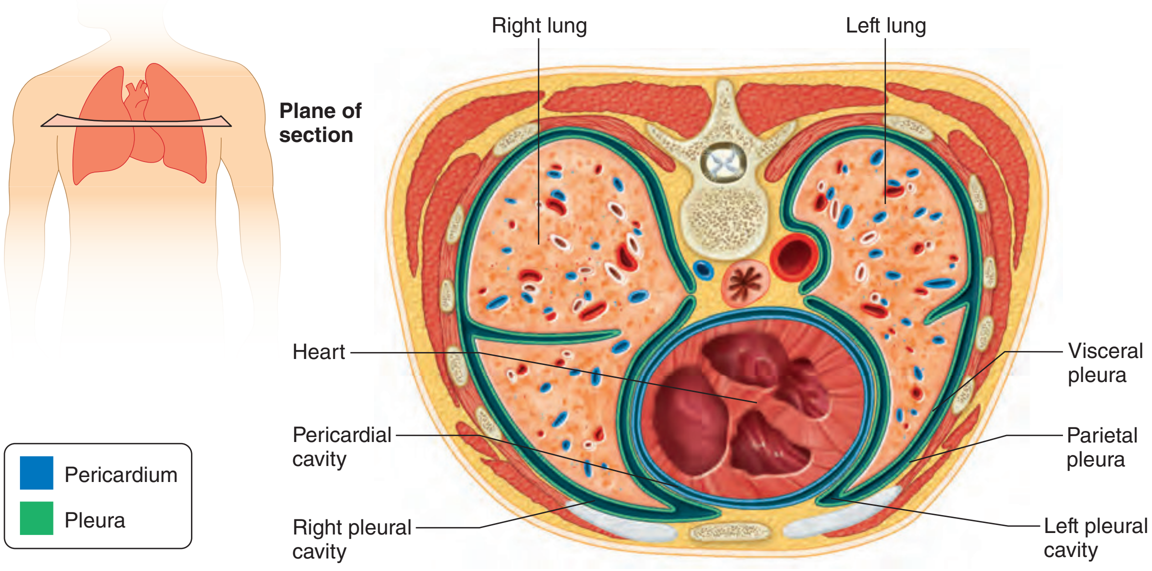


**FIGURE 16.11** The potential spaces between the pleural membranes, called the left and right pleural cavities, are shown here as actual spaces.

mercury about 760 millimeters (mm) high in a tube. Thus, normal air pressure is equal to 760 mm of mercury (Hg).

Air pressure is exerted on all surfaces in contact with the air, and because people breathe air, the inside surfaces of their lungs also are subjected to pressure. The pressures on the inside of the lungs and alveoli and on the outside of the thoracic wall are about the same.

Pressure and volume are related in an opposite (inverse) way. For example, pulling back on the plunger of a syringe increases the volume inside the barrel and decreases the air pressure inside. Atmospheric pressure then pushes outside air into the syringe. In contrast, pushing on the plunger reduces the volume inside the syringe, but the pressure inside increases, forcing air out into the atmosphere. The movement of air into and out of the lungs occurs in much the same way.

If the pressure inside the lungs and alveoli decreases, atmospheric pressure will push outside air into the airways. That is what happens during normal inspiration. Impulses conducted on the phrenic nerves, which are associated with the cervical plexuses (see chapter 9, p. 262), stimulate muscle fibers in the dome-shaped *diaphragm* below the lungs to contract. The diaphragm moves downward, the thoracic cavity enlarges, and the pressure in the alveoli (intra-alveolar pressure) falls to about 2 mm Hg below that of atmospheric pressure. In response, atmospheric pressure forces air into the airways (fig. 16.12).

While the diaphragm is contracting and moving downward, the *external (inspiratory) intercostal muscles* between the ribs may be stimulated to contract. This action moves the ribs and the sternum upward and outward, enlarging the thoracic cavity even more. As a result, the intra-alveolar pressure is reduced further, and the greater atmospheric pressure forces even more air into the alveoli.

Lung expansion in response to movements of the diaphragm and chest wall depends on movements of the pleural membranes. Any separation of the pleural membranes decreases pressure in the intrapleural space, resisting further separation and holding these membranes together. In addition, only a thin film of serous fluid separates the parietal pleura on the inner wall of the thoracic cavity from the visceral pleura attached to the surface of the lungs. The water molecules in this fluid are attracted to the pleural membranes and to each other, helping to adhere the moist surfaces of the pleural membranes, much as a wet coverslip sticks to a microscope slide. As a result of these factors, when the external intercostal muscles move the thoracic wall upward and outward, the parietal pleura moves too, and the visceral pleura follows it. This helps expand the lung in all directions.

The moist pleural membranes play a role in expanding the lungs, but the moist inner surfaces of the alveoli have the opposite effect. In the alveoli, the attraction of water molecules creates a force called **surface tension** that makes it difficult to inflate the alveoli and may actually collapse them. Certain alveolar cells, however, synthesize a mixture of lipids and proteins called **surfactant** (ser-fak′tant). It is secreted continuously into alveolar air spaces and reduces the alveoli's tendency to collapse, especially when lung volumes are low. Surfactant makes it easier for inspiratory efforts to expand the alveoli.

Surfactant is particularly important in the minutes after birth, when the newborn's lungs fully inflate for the first time. Premature infants may suffer respiratory distress syndrome if they do not produce sufficient surfactant. To help many of these newborns survive, physicians introduce synthetic surfactant into the tiny lungs through an endotracheal tube. A ventilator machine especially geared to an infant's size assists breathing.

If a person needs to take a deeper than normal breath, the diaphragm and external intercostal muscles contract more forcefully. Additional muscles, such as the pectoralis minor, the sternocleidomastoid, and the scalenes, can also pull the thoracic cage farther upward and outward, enlarging the thoracic cavity and further decreasing intra-alveolar pressure (fig. 16.13).

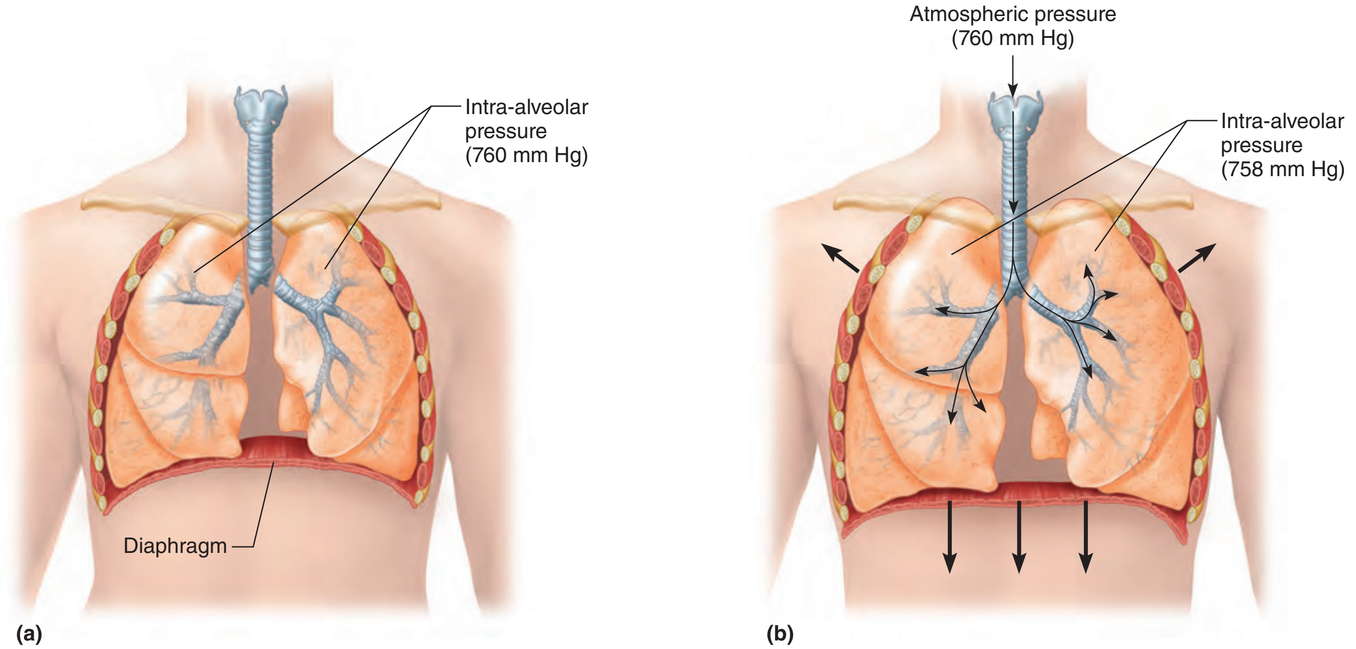


**FIGURE 16.12** APR Normal inspiration. **(a)** Prior to inspiration, the intra-alveolar pressure is 760 mm Hg. **(b)** The intra-alveolar pressure decreases to about 758 mm Hg as the thoracic cavity enlarges, and atmospheric pressure forces air into the airways.

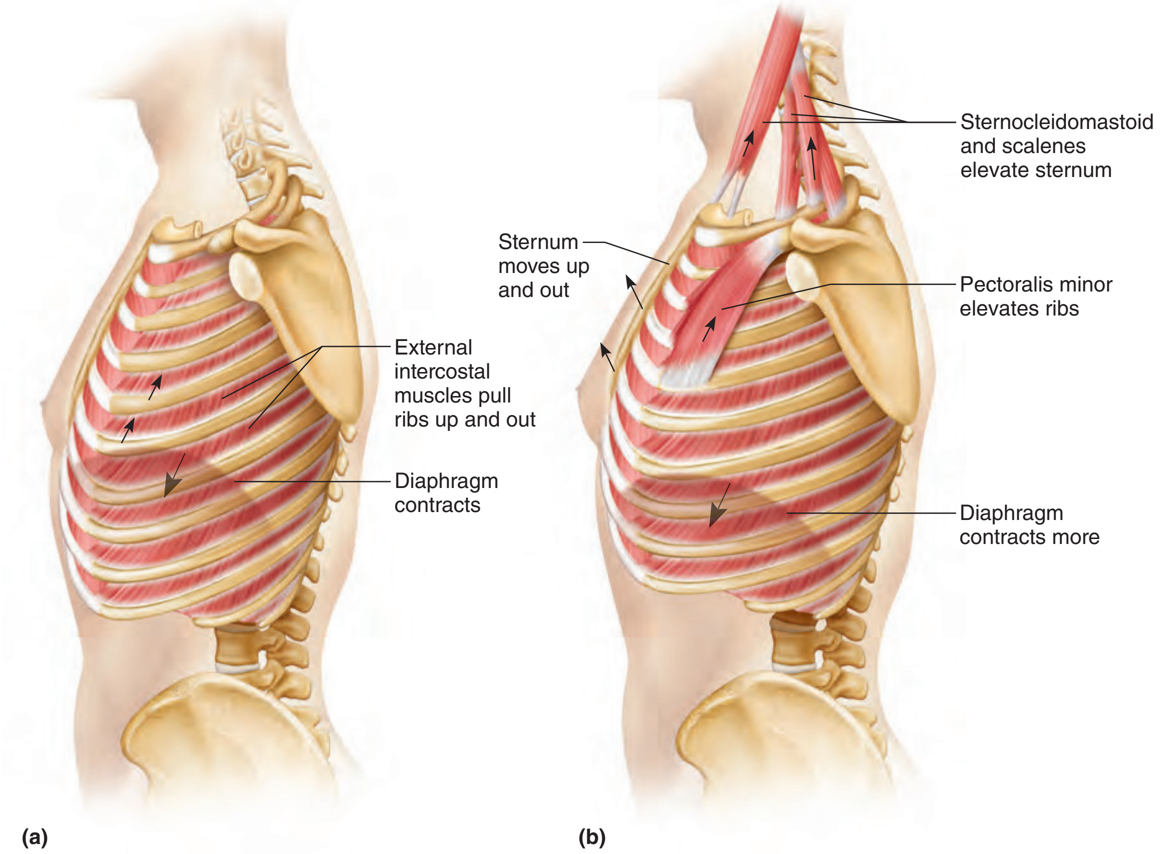

External intercostal muscles pull ribs up and out
Diaphragm contracts
Sternum moves up and out
Sternocleidomastoid and scalenes elevate sternum
Pectoralis minor elevates ribs
Diaphragm contracts more
(a)
(b)

**FIGURE 16.13** Maximal inspiration. **(a)** Shape of the thorax at the end of normal inspiration. **(b)** Shape of the thorax at the end of maximal inspiration, aided by contraction of the sternocleidomastoid and pectoralis minor muscles.

**FACTS OF LIFE** The first breath is the toughest. A newborn must use twenty times the energy to take the first breath as for subsequent breaths.

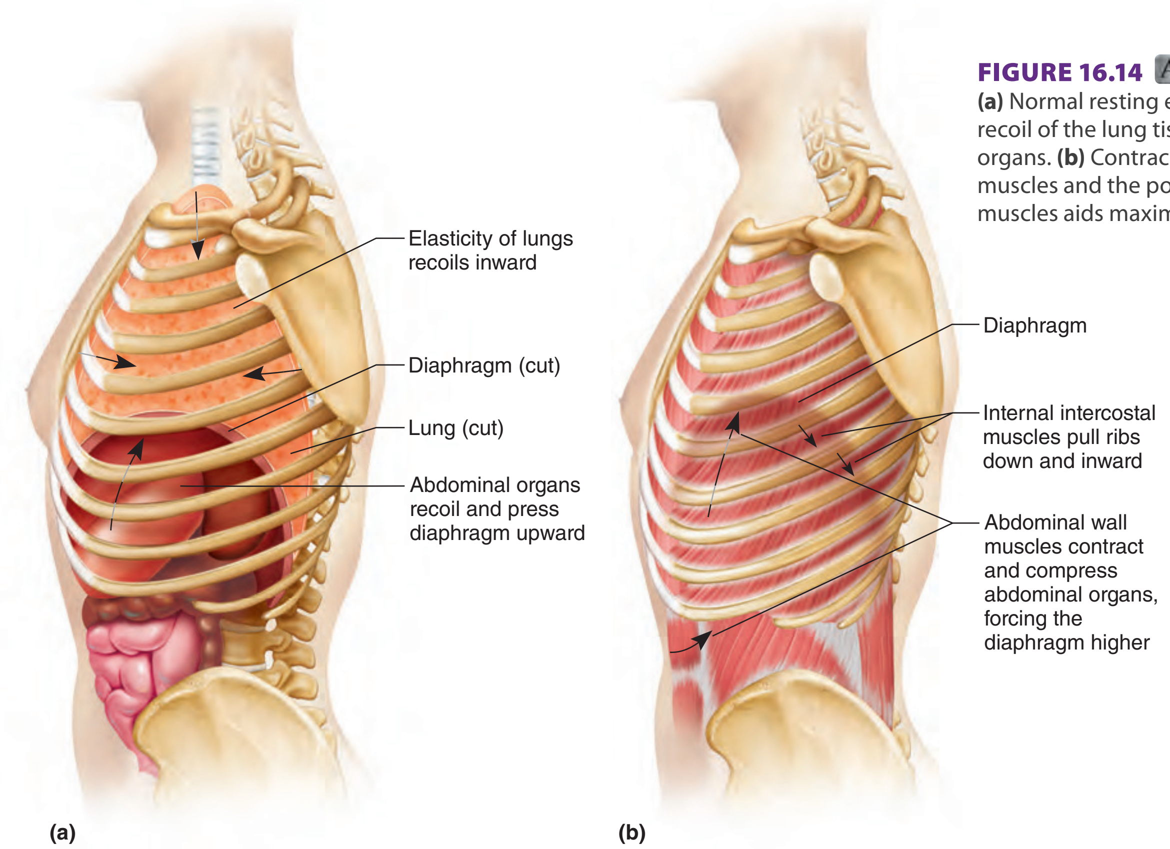
## Expiration

The forces for resting expiration come from the *elastic recoil* of tissues and from surface tension. The lungs and thoracic wall contain considerable elastic tissue, which stretches with lung expansion during inspiration. Also, the diaphragm lowering compresses the abdominal organs beneath it. As the diaphragm and external intercostal muscles relax following inspiration, the elastic tissues cause the lungs and thoracic cage to recoil and return to their original shapes. Similarly, the abdominal organs spring back into their previous shapes, pushing the diaphragm upward (fig. 16.14*a*). At the same time, the surface tension that develops between the moist surfaces of the alveolar linings decreases the diameters of the alveoli. Each of these factors increases intra-alveolar pressure about 1 mm Hg above atmospheric pressure, so that the air inside the lungs is forced out through respiratory passages. Thus, normal resting expiration is a passive process.

Low pressure and wet surfaces hold the visceral and parietal pleural membranes together, so no actual space normally exists in the pleural cavity between them. However, a puncture in the thoracic wall admits atmospheric air into the pleural cavity and creates a real space between the membranes. This condition, called *pneumothorax,* may collapse the lung on the affected side because of the lung's elasticity. A collapsed lung is called *atelectasis*.

If a person needs to exhale more air than normal the posterior *internal (expiratory) intercostal muscles* can contract (fig. 16.14*b*). These muscles pull the ribs and sternum downward and inward, increasing the air pressure in the lungs to force more air out. Also, the *abdominal wall muscles,* including the external and internal obliques, transversus abdominis, and rectus abdominis, can squeeze the abdominal organs inward (see fig. 8.19, p. 209). In this way, the abdominal wall muscles can increase pressure in the abdominal cavity and force the diaphragm still higher against the lungs. These actions force additional air out of the lungs. Clinical Application 16.1 discusses problems in breathing associated with two common diseases, emphysema and lung cancer.

**FIGURE 16.14** APR Expiration. **(a)** Normal resting expiration is due to elastic recoil of the lung tissues and the abdominal organs. **(b)** Contraction of the abdominal wall muscles and the posterior internal intercostal muscles aids maximal expiration.


Elasticity of lungs recoils inward
Diaphragm (cut)
Lung (cut)
Abdominal organs recoil and press diaphragm upward
(a)
Diaphragm
Internal intercostal muscles pull ribs down and inward
Abdominal wall muscles contract and compress abdominal organs, forcing the diaphragm higher
(b)

Air movements other than breathing are called *nonrespiratory movements*. They are used to clear air passages, as in coughing and sneezing, or to express emotion, as in laughing and crying.

Nonrespiratory movements usually result from *reflexes,* although sometimes they are initiated voluntarily. A *cough,* for example, can be produced through conscious effort or may be triggered by a foreign object in an air passage.

Coughing involves taking a deep breath, closing the glottis, and forcing air upward from the lungs against the closure. Then the glottis is suddenly opened, and a blast of air is forced upward from the lower respiratory tract. Usually, this rapid rush of air removes the substance that triggered the reflex.

A *sneeze* is much like a cough, but it clears the upper respiratory passages rather than the lower ones. This reflex is usually initiated by a mild irritation in the lining of the nasal cavity, and in response, a blast of air is forced up through the glottis. The air is directed into the nasal passages by depressing the uvula, closing the opening between the pharynx and the oral cavity. A sneeze can propel a particle out of the nose at 200 miles per hour.

*Laughing* involves taking a breath and releasing it in a series of short expirations. *Crying* consists of very similar movements. It may be necessary to note a person's facial expression to distinguish laughing from crying.

A *hiccup* is caused by sudden inspiration due to a spasmodic contraction of the diaphragm while the glottis is closed. Air striking the vocal folds generates the sound of the hiccup. We do not know the function, if any, of hiccups.

*Yawning* is familiar to everyone, yet its significance and how it is contagious remain poorly understood. Evidence points away from a role in increasing oxygen intake, as had long been thought.

**PRACTICE**

15. Describe the events in inspiration.
16. How does expansion of the chest wall expand the lungs during inspiration?
17. Which forces cause normal expiration?

## Respiratory Air Volumes and Capacities

Different efforts in breathing move different volumes of air in or out of the lungs. *Spirometry* is a test that measures such air volumes. Three distinct **respiratory volumes** (re-spi′rah-to″re vol′ūmz) can be measured using spirometry and a fourth (residual volume) cannot.

One inspiration plus the following expiration is called a **respiratory cycle.** The volume of air that enters (or leaves) during a single respiratory cycle is termed the **tidal volume.** About 500 milliliters (mL) of air enter during a normal, resting inspiration. Approximately the same volume leaves during a normal, resting expiration. Thus, the **resting tidal volume** is about 500 mL (fig. 16.15).

During forced inspiration, air in addition to the resting tidal volume enters the lungs. This extra volume is the **inspiratory reserve volume** (complemental air), and at maximum, it equals about 3,000 mL.

During forced expiration, the lungs can expel up to about 1,100 mL of air beyond the resting tidal volume. This volume is called the **expiratory reserve volume** (supplemental air). However, even after the most forceful

## CLINICAL APPLICATION 16.1

## Emphysema and Lung Cancer

*Emphysema* is a progressive, degenerative disease that destroys alveolar walls. As a result, clusters of small air sacs merge into larger chambers, which greatly decreases the surface area of the respiratory membrane, thereby reducing the volume of gases that can be exchanged through the membrane. Alveolar walls lose some of their elasticity, and capillary networks associated with the alveoli diminish (fig. 16A). Loss of tissue elasticity in the lungs contributes to making it increasingly difficult for a person with emphysema to exhale.

Emphysema may develop in response to prolonged exposure to respiratory irritants, such as those in tobacco smoke and polluted air. The disease may also result from an inherited enzyme (alpha-1 antitrypsin) deficiency. Emphysema is a type of chronic obstructive pulmonary disease (COPD).

*Lung cancer,* like other cancers, is the uncontrolled division of abnormal cells that rob normal cells of nutrients and oxygen, eventually crowding them out. Some cancerous growths in the lungs result secondarily from cancer cells that have spread (metastasized) from other parts of the body, such as the breasts, intestines, liver, or kidneys. Cancers that begin in the lungs are called *primary pulmonary cancers*. These may arise from epithelia, connective tissue, or blood cells. The most common form originates from epithelium in a bronchiole (fig. 16B) and is called *bronchogenic carcinoma*. This type of cancer is a response to irritation, such as prolonged exposure to tobacco smoke. Susceptibility to primary pulmonary cancers may be inherited.

Cancer cells divide to form tumor masses that obstruct air passages and reduce gas exchange. Bronchogenic carcinoma can spread quickly, establishing secondary cancers in the lymph nodes, liver, bones, brain, or kidneys. Lung cancer is treated with surgery, ionizing radiation, and drugs, but the survival rate is low.

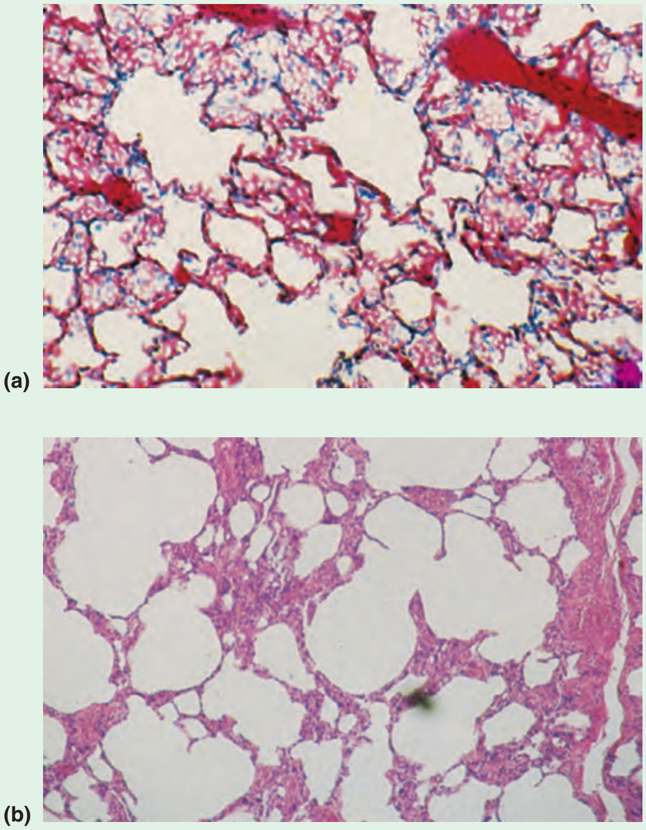


**FIGURE 16A** Comparison of lung tissues. **(a)** Normal lung tissue (100×). **(b)** As emphysema develops, alveoli merge, forming larger chambers (100×).

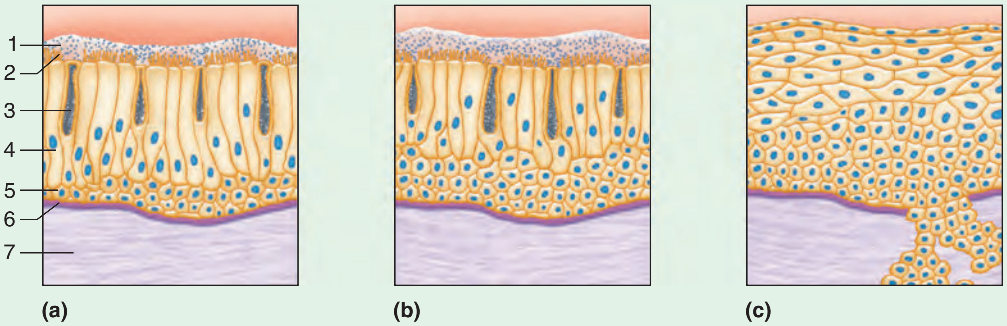


**FIGURE 16B** About 95% of lung cancers start in the lining (epithelium) of a bronchiole. **(a)** The normal lining shows (**4**) columnar cells with (**2**) hairlike cilia, (**3**) goblet cells that secrete (**1**) mucus, and (**5**) basal cells from which new columnar cells arise. (**6**) A basement membrane separates the epithelial cells from (**7**) the underlying connective tissue. **(b)** In the first stage of lung cancer, the basal cells divide repeatedly. The goblet cells secrete excess mucus, and the cilia are less efficient in moving the heavy mucus secretion. **(c)** Continued division of basal cells displaces the columnar and goblet cells. The basal cells penetrate the basement membrane and invade the deeper connective tissue.

expiration, about 1,200 mL of air remains in the lungs. This is called the **residual volume** and can only be measured using special gas dilution techniques.

Because of the residual volume and the expiratory reserve volumes, newly inhaled air always mixes with air already in the lungs. This prevents the oxygen and carbon dioxide concentrations in the lungs from fluctuating greatly with each breath.

Four **respiratory capacities** (re-spi′rah-to″re kah-pas′ĭ-tēz) can be determined by combining two or more of the respiratory volumes. Combining the inspiratory reserve volume (3,000 mL) with the tidal volume (500 mL) and the expiratory reserve volume (1,100 mL) gives the **vital capacity** (4,600 mL). This is the maximum volume of air a person can exhale after taking the deepest breath possible.

The tidal volume (500 mL) plus the inspiratory reserve volume (3,000 mL) gives the **inspiratory capacity** (3,500 mL). This is the maximum volume of air a person can inhale following a resting expiration. Similarly, the expiratory reserve volume (1,100 mL) plus the residual volume (1,200 mL) equals the **functional residual capacity** (2,300 mL). This is the volume of air that remains in the lungs following a resting expiration.

The vital capacity plus the residual volume equals the **total lung capacity** (about 5,800 mL). This total varies with age, sex, and body size.

Some of the air that enters the respiratory tract during breathing does not reach the alveoli. This volume (about 150 mL) remains in the passageways of the trachea, bronchi, and bronchioles. Because gas is not exchanged through the walls of these passages, this air is said to occupy *anatomic dead space.* Table 16.2 summarizes the respiratory air volumes and capacities.

An instrument called a *spirometer* measures respiratory air volumes, except residual volume, which requires a special technique. Such measurements are used to help evaluate the courses of emphysema, pneumonia, and lung cancer, conditions in which functional lung tissue is lost. Spirometry may also be used to track the progress of diseases, such as bronchial asthma, that obstruct air passages.

## TABLE 16.2 Respiratory Air Volumes and Capacities

| Name | Volume* | Description |
|---|---|---|
| Tidal volume (TV) | 500 mL | Volume of air moved in or out of the lungs during a respiratory cycle |
| Inspiratory reserve volume (IRV) | 3,000 mL | Maximal volume of air that can be inhaled after a resting inspiration |
| Expiratory reserve volume (ERV) | 1,100 mL | Maximal volume of air that can be exhaled after a resting expiration |
| Residual volume (RV) | 1,200 mL | Volume of air that remains in the lungs after a maximal expiration |
| Inspiratory capacity (IC) | 3,500 mL | Maximum volume of air that can be inhaled following exhalation of tidal volume: IC = TV + IRV |
| Functional residual capacity (FRC) | 2,300 mL | Volume of air that remains in the lungs following exhalation of tidal volume: FRC = ERV + RV |
| Vital capacity (VC) | 4,600 mL | Maximum volume of air that can be exhaled after taking the deepest breath possible: VC = TV + IRV + ERV |
| Total lung capacity (TLC) | 5,800 mL | Total volume of air that the lungs can hold: TLC = VC + RV |

*Values are typical for a tall, young adult.

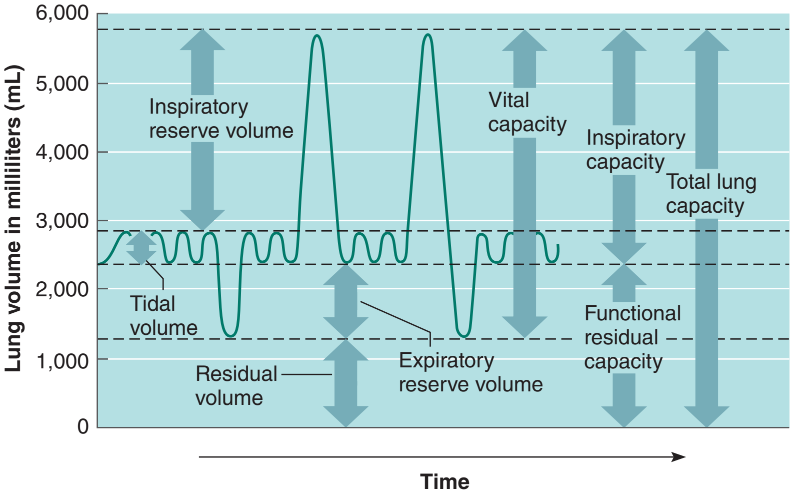


**FIGURE 16.15** Respiratory volumes and capacities.

Q *During inspiration, which way would the pen move in this figure?*

**Answer can be found in Appendix F on page 582.**

## PRACTICE

18. What is tidal volume?
19. Distinguish between inspiratory and expiratory reserve volumes.
20. How is vital capacity determined?
21. How is total lung capacity calculated?

## 16.4 | Control of Breathing

Normal breathing is a rhythmic, involuntary act that continues even when a person is unconscious. The respiratory muscles, however, are also under voluntary control. (Take a deep breath and consider this!)

### Respiratory Areas

Groups of neurons in the brainstem form the **respiratory areas,** which control both inspiration and expiration. The components of the respiratory areas are widely distributed throughout the pons and medulla oblongata. Two parts of the respiratory areas are of special interest: the respiratory center of the medulla and the respiratory group of the pons (fig. 16.16).

The **medullary respiratory center** includes two bilateral groups of neurons that extend throughout the length of the medulla oblongata. They are called the ventral respiratory group and the dorsal respiratory group.

Current evidence suggests that the basic rhythm of breathing arises from the *ventral respiratory group.*

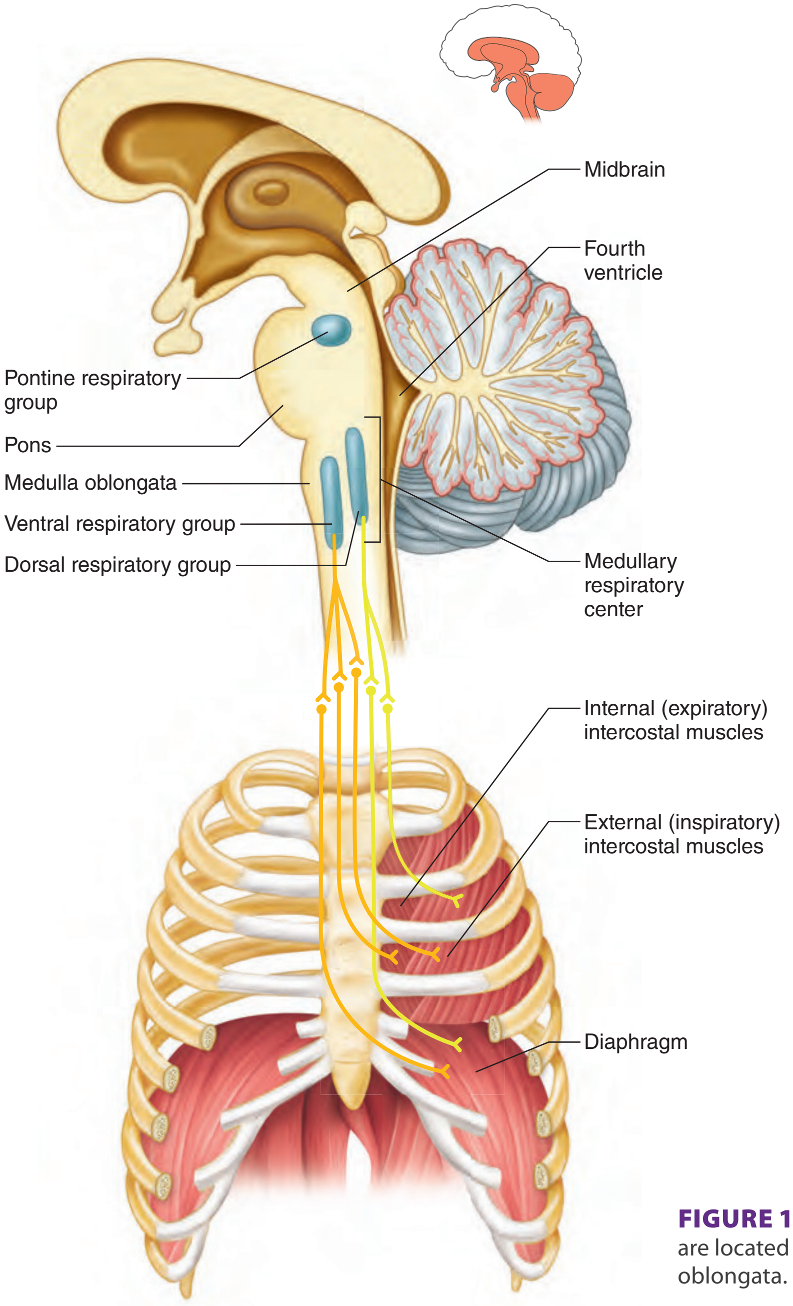

Midbrain
Fourth ventricle
Pontine respiratory group
Pons
Medulla oblongata
Ventral respiratory group
Dorsal respiratory group
Medullary respiratory center
Internal (expiratory) intercostal muscles
External (inspiratory) intercostal muscles
Diaphragm

**FIGURE 16.16** The respiratory areas are located in the pons and the medulla oblongata.

The *dorsal respiratory group* stimulates the inspiratory muscles, primarily the diaphragm. The dorsal respiratory group also helps process sensory information regarding the respiratory system and may play a role in certain cardiopulmonary reflexes that affect respiratory rhythm (fig. 16.17).

Neurons in another part of the brainstem, the pons, form the *pontine respiratory group* (formerly called the *pneumotaxic center*). They may contribute to the rhythm of breathing by limiting inspiration.

### PRACTICE

22. Where are the respiratory areas?
23. Describe how the respiratory areas maintain a normal breathing pattern.
24. Explain how the breathing pattern may change.

## Factors Affecting Breathing

The respiratory areas affect breathing rate and depth, and so do certain chemicals in body fluids, the degree to which lung tissues stretch, a person's emotional state, and level of physical activity (Clinical Application 16.2). For example, *chemosensitive areas* (central chemoreceptors) in the ventral part of the medulla oblongata near the origins of the vagus nerves sense changes in the cerebrospinal fluid (CSF) levels of carbon dioxide and hydrogen ions. If either level rises, the central chemoreceptors signal the respiratory areas, and respiratory rate and tidal volume increase. As a result of the increased ventilation, more carbon dioxide is exhaled, the blood and CSF levels of these chemicals fall, and breathing rate decreases.

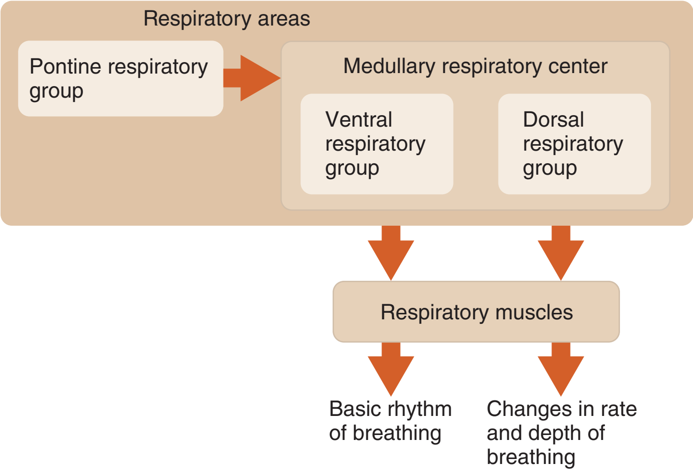

Respiratory areas
Pontine respiratory group
Medullary respiratory center
Ventral respiratory group
Dorsal respiratory group
Respiratory muscles
Basic rhythm of breathing
Changes in rate and depth of breathing

**FIGURE 16.17** The medullary respiratory center and the pontine respiratory group control breathing.

Adding carbon dioxide to air can stimulate the rate and depth of breathing. Ordinary air is about 0.04% carbon dioxide. Inhaling air containing 4% carbon dioxide usually doubles the breathing rate.

Low blood oxygen has little direct effect on the central chemoreceptors associated with the respiratory areas. Instead, *peripheral chemoreceptors* in specialized structures called the *carotid bodies* and the *aortic bodies* sense changes in blood oxygen levels. Peripheral chemoreceptors are in the walls of certain large arteries (the carotid arteries and the aorta) in the neck and thorax (fig. 16.18). Stimulated peripheral chemoreceptors initiate impulses to the respiratory areas, increasing the breathing rate. However, blood oxygen levels must be very low to trigger this mechanism. Thus, oxygen plays only a minor role in the control of normal respiration.

An *inflation reflex* helps regulate the depth of breathing. This reflex occurs when stretched lung tissues stimulate stretch receptors in the visceral pleura, bronchioles, and alveoli. The sensory impulses of this reflex travel via the vagus nerves to the pontine respiratory group and shorten the duration of inspiratory movements. This action prevents overinflation of the lungs during forceful breathing.

Emotional upset can alter the normal breathing pattern. Fear and pain typically increase the breathing rate. Conscious control of breathing is also possible because the respiratory muscles are voluntary.

A person can voluntarily stop breathing for a very short time. If breathing stops, blood levels of carbon dioxide and hydrogen ions rise, and oxygen levels fall. These changes (primarily the increased carbon dioxide) stimulate the chemoreceptors, and soon the urge to inhale overpowers the desire to hold the breath.

A person can increase breath-holding time by breathing rapidly and deeply enough in advance to exhale excess carbon dioxide. This action, called **hyperventilation** (hi″per-ven″tĭ-la′shun), lowers the blood carbon dioxide level. Following hyperventilation, it takes longer for carbon dioxide to rise to the level that stimulates the respiratory areas. (*Note:* Prolonging breath-holding in this way can cause abnormally low blood oxygen levels. Use of hyperventilation to help hold the breath while swimming is potentially dangerous because the person may lose consciousness underwater and drown.)

Interference with the oxygen supply to the brain may cause fainting. A person who is emotionally upset may hyperventilate, become dizzy, and lose consciousness. This condition is due to a lowered carbon dioxide concentration followed by a rise in pH (alkalosis), a localized vasoconstriction of cerebral arterioles, and resulting decreased blood flow to nearby brain cells.

### CLINICAL APPLICATION 16.2

## Exercise and Breathing

Moderate to heavy physical exercise greatly increases the volume of oxygen the skeletal muscles use. For example, a young man at rest utilizes about 250 mL of oxygen per minute, but maximal exercise may require 3,600 mL of oxygen per minute.

As oxygen utilization increases, the volume of carbon dioxide produced also increases. Because decreased blood oxygen and increased blood carbon dioxide concentrations stimulate the respiratory areas, exercise would be expected to increase breathing rate. Studies reveal, however, that blood oxygen and carbon dioxide concentrations usually do not change significantly during exercise.

Sensory structures called *proprioceptors* that are associated with muscles and joints cause much of the increased breathing rate during vigorous exercise. Muscular movements stimulate proprioceptors, triggering a *joint reflex* that sends impulses to the respiratory center, increasing breathing rate.

When breathing rate increases during exercise, increased blood flow is also required to power skeletal muscles. Thus, physical exercise taxes both the cardiovascular and respiratory systems. If either of these systems does not keep pace with cellular demands, the person feels short of breath. This feeling may reflect an inability of the heart and blood vessels to move enough blood between the lungs and cells, or the respiratory system's inability to provide enough air.

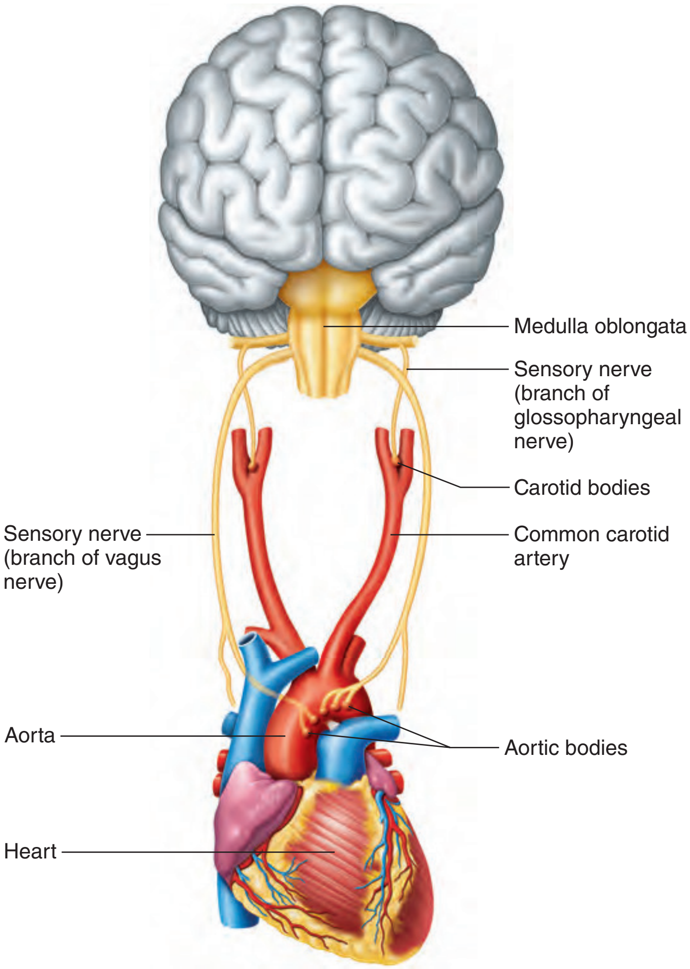

Medulla oblongata
Sensory nerve (branch of glossopharyngeal nerve)
Carotid bodies
Common carotid artery
Sensory nerve (branch of vagus nerve)
Aorta
Aortic bodies
Heart

**FIGURE 16.18** Decreased blood oxygen concentration stimulates peripheral chemoreceptors in the carotid and aortic bodies.

### PRACTICE

25. Which chemical factors affect breathing?
26. Describe the inflation reflex.
27. How does hyperventilation decrease the respiratory rate?

## 16.5 | Alveolar Gas Exchanges

The parts of the respiratory system discussed so far conduct air in and out of air passages. The alveoli carry on the vital process of exchanging gases between the air and the blood.

### Alveoli

Alveoli are microscopic air sacs clustered at the distal ends of the narrowest respiratory tubes, the alveolar ducts (see fig. 16.8). Each alveolus consists of a tiny space within a thin wall that separates it from adjacent alveoli.

### Respiratory Membrane

The wall of an alveolus is simple squamous epithelium. In close association with an alveolus is a dense network of capillaries, which also have walls of simple squamous epithelium. Thin, fused basement membranes separate the layers of these flattened cells, and in the spaces between the cells are elastic and collagen fibers that support the alveolar wall. At least two thicknesses of epithelial cells and a layer of fused basement membranes separate the air in an alveolus from the blood in a capillary. These layers constitute the **respiratory membrane** (re-spi′rah-to″re mem′brān) across which blood and alveolar air exchange gases (fig. 16.19).

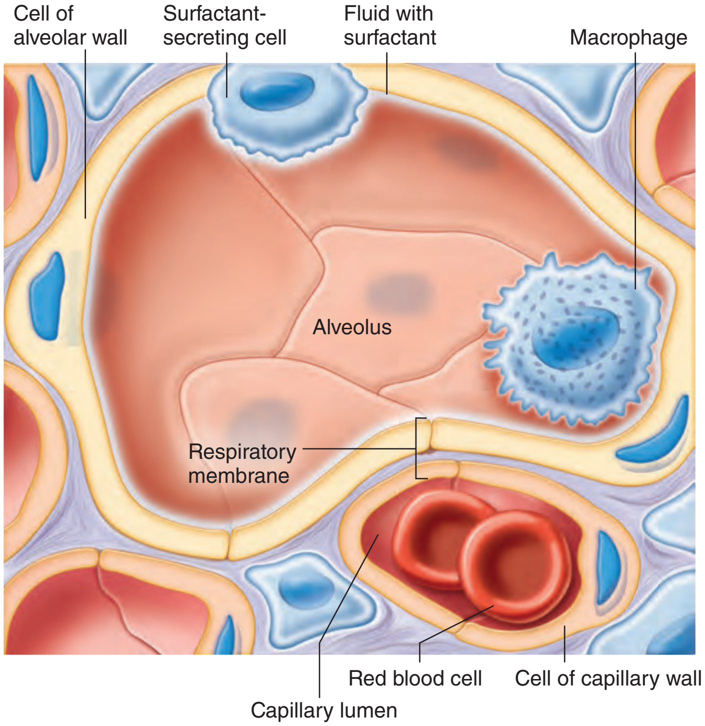

Cell of alveolar wall
Surfactant-secreting cell
Fluid with surfactant
Macrophage
Alveolus
Respiratory membrane
Red blood cell
Cell of capillary wall
Capillary lumen

**FIGURE 16.19** The respiratory membrane consists of the wall of the alveolus and the wall of the capillary.

**FACTS OF LIFE** If all of the capillaries that surround the alveoli were unwound and laid end to end, they would extend for about 600 miles.

## Diffusion Across the Respiratory Membrane

Measured by volume, ordinary air is about 78% nitrogen, 21% oxygen, and 0.04% carbon dioxide. Air also has traces of other gases that have little or no physiological importance.

In a mixture of gases such as air, each gas accounts for a portion of the total pressure the mixture produces. The amount of pressure each gas contributes is called the **partial pressure** (par′shal presh′ur) of that gas and is proportional to its concentration. For example, because air is 21% oxygen, oxygen accounts for 21% of the atmospheric pressure (21% of 760 mm Hg), or 160 mm Hg. Thus, the partial pressure of oxygen, symbolized $P_{O_2}$, in atmospheric air is 160 mm Hg. Similarly, the partial pressure of carbon dioxide ($P_{CO_2}$) in air is 0.3 mm Hg.

Gas molecules from the air may enter, or dissolve in, a liquid. This happens when carbon dioxide is added to a carbonated beverage, or when inspired gases dissolve in the blood in the alveolar capillaries. The partial pressure of a gas exposed to a liquid determines how much dissolves. For example, when a mixture of gases dissolves in blood, the resulting concentration of each gas is proportional to its partial pressure.

Recall from chapter 3 (pp. 70–73) that molecules diffuse from regions where they are in higher concentration toward regions where they are in lower concentration. The same principle applies to diffusion of dissolved gases, but for dissolved gases, it is more useful to think of diffusion from regions of higher partial pressure toward regions of lower partial pressure. Each gas diffuses between blood and its surroundings from areas of higher partial pressure to areas of lower partial pressure until the partial pressures in the two regions reach equilibrium. For example, the $P_{CO_2}$ in capillary blood is 45 mm Hg, but the $P_{CO_2}$ in alveolar air is 40 mm Hg. Because of the difference in these partial pressures, carbon dioxide diffuses from blood, where its partial pressure is higher, across the respiratory membrane and into alveolar air (fig. 16.20). When blood leaves the lungs, its $P_{CO_2}$ is 40 mm Hg, which is the same as the $P_{CO_2}$ of alveolar air. Similarly, the $P_{O_2}$ of capillary blood is 40 mm Hg, but that of alveolar air is 104 mm Hg. Thus, oxygen diffuses from alveolar air into blood, and blood leaves the lungs with a $P_{O_2}$ of 104 mm Hg. (Because of the relatively large volume of air always in the lungs, as long as breathing continues, alveolar $P_{O_2}$ stays relatively constant at 104 mm Hg.)

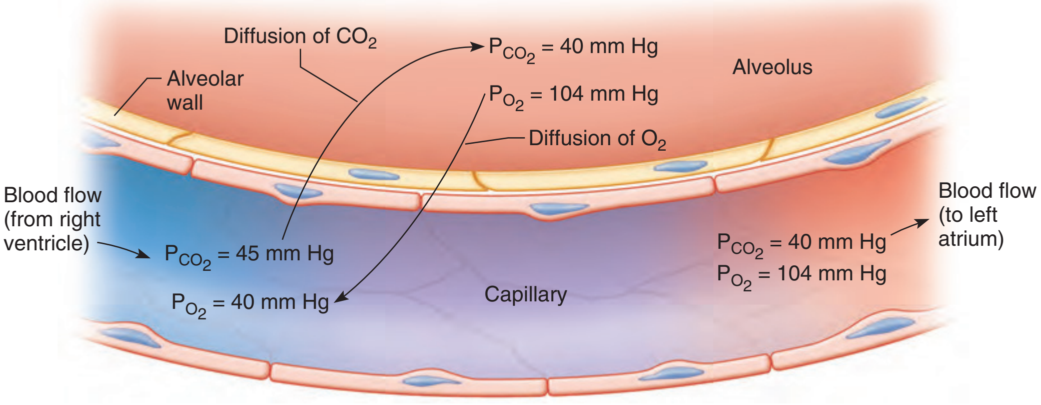

Diffusion of $CO_2$
$P_{CO_2}$ = 40 mm Hg
Alveolus
Alveolar wall
$P_{O_2}$ = 104 mm Hg
Diffusion of $O_2$
Blood flow (from right ventricle)
$P_{CO_2}$ = 45 mm Hg
$P_{O_2}$ = 40 mm Hg
Capillary
$P_{CO_2}$ = 40 mm Hg
$P_{O_2}$ = 104 mm Hg
Blood flow (to left atrium)

**FIGURE 16.20** Gases are exchanged between alveolar air and capillary blood because of differences in partial pressures.

A number of factors affect diffusion across the respiratory membrane. More surface area, shorter distance, greater solubility of gases, and a steeper partial pressure gradient all favor increased diffusion. Thus, diseases that harm the respiratory membrane, such as pneumonia, or diseases that reduce the surface area for diffusion, such as emphysema, may require increased $Po_2$ for treatment.

The respiratory membrane is normally so thin that certain soluble chemicals other than carbon dioxide may diffuse into alveolar air and be exhaled. This is why breath analysis can reflect alcohol in the blood of one who has been drinking, or reveal acetone on the breath of a person who has untreated diabetes mellitus. Breath analysis may also detect substances associated with kidney failure, certain digestive disturbances, and liver disease. A breath analysis is also called a "breathprint" because studies show it is unique to an individual, as is a fingerprint.

## PRACTICE

28. Describe the structure of the respiratory membrane.
29. What is the partial pressure of a gas?
30. Which force moves oxygen and carbon dioxide across the respiratory membrane?

## 16.6 | Gas Transport

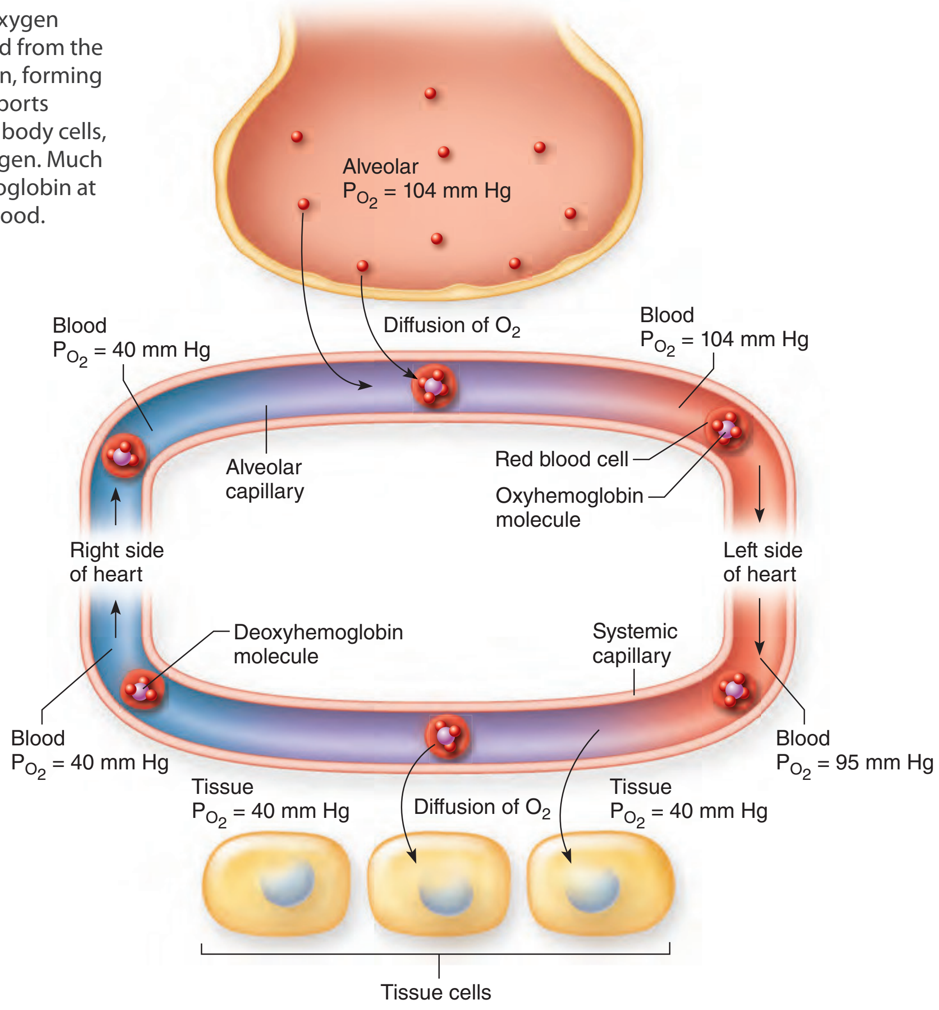
Blood transports oxygen and carbon dioxide between the lungs and the cells. As these gases enter blood, they dissolve in the liquid portion (plasma) or combine chemically with blood components.

### Oxygen Transport

Almost all the oxygen (over 98%) that blood transports binds the iron-containing protein **hemoglobin** (he″mo-glo′bin) in red blood cells. The remainder of the oxygen dissolves in plasma.

In the lungs, where the $Po_2$ is relatively high, oxygen dissolves in blood and combines rapidly with the iron atoms of hemoglobin, forming **oxyhemoglobin** (ok″sĭ-he″mo-glo′bin). Each hemoglobin molecule can bind up to four oxygen molecules. (fig. 16.21). Notice that although blood leaves the alveolar capillaries with a $PO_2$ of 104 mm Hg, it enters the systemic capillaries with a $PO_2$ of 95 mm Hg. This difference in partial pressure occurs because venous blood draining the bronchi and bronchioles mixes with pulmonary venous blood before returning to the heart. As a result,

**FIGURE 16.21** APR Oxygen molecules, entering the blood from the alveolus, bond to hemoglobin, forming oxyhemoglobin. Blood transports oxygen. In the regions of the body cells, oxyhemoglobin releases oxygen. Much oxygen is still bound to hemoglobin at the $Po_2$ of systemic venous blood.


Alveolar
$P_{O_2}$ = 104 mm Hg
Diffusion of $O_2$
Blood
$P_{O_2}$ = 40 mm Hg
Blood
$P_{O_2}$ = 104 mm Hg
Alveolar capillary
Red blood cell
Oxyhemoglobin molecule
Right side of heart
Left side of heart
Deoxyhemoglobin molecule
Systemic capillary
Blood
$P_{O_2}$ = 40 mm Hg
Blood
$P_{O_2}$ = 95 mm Hg
Tissue
$P_{O_2}$ = 40 mm Hg
Diffusion of $O_2$
Tissue
$P_{O_2}$ = 40 mm Hg
Tissue cells

the $PO_2$ of left atrial, left ventricular, and systemic arterial blood is 95 mm Hg.

The chemical bonds between oxygen and hemoglobin molecules can break. In regions of body cells, where the $Po_2$ decreases, oxyhemoglobin molecules release oxygen, which diffuses into nearby cells that have depleted their oxygen supplies in cellular respiration (fig. 16.21).

Several other factors affect how much oxygen oxyhemoglobin releases. More oxygen is released as the blood concentration of carbon dioxide increases, as blood becomes more acidic, or as blood temperature increases. This explains why more oxygen is released from oxyhemoglobin to skeletal muscles during physical exercise. The increased muscular activity and oxygen utilization increase carbon dioxide concentration, decrease pH, and raise temperature. Less active cells receive proportionately less oxygen.

A deficiency of $O_2$ reaching the tissues is called **hypoxia.** It may be a response to decreased arterial $Po_2$ (*hypoxemia*), diminished ability of the blood to transport $O_2$ (anemic hypoxia), inadequate blood flow (ischemic hypoxia), or a defect at the cellular level (histotoxic hypoxia), such as in cyanide poisoning.

## PRACTICE

31. How is oxygen transported from the lungs to cells?
32. What stimulates blood to release oxygen to tissues?

## Carbon Dioxide Transport

Blood flowing through capillaries gains carbon dioxide because tissues have a relatively high $Pco_2$. Blood transports carbon dioxide to the lungs in one of three forms: as carbon dioxide dissolved in plasma, as part of a compound formed by bonding to hemoglobin, or as a bicarbonate ion (fig. 16.22).

The amount of carbon dioxide that dissolves in plasma is determined by its partial pressure. The higher the $Pco_2$ of the tissues, the more carbon dioxide will go into solution. However, only about 7% of the carbon dioxide that blood transports is in this form.

Unlike oxygen, which binds the iron atoms (part of the "heme" portion) of hemoglobin molecules, carbon dioxide bonds with the amino groups ($-NH_2$) of the "globin" or protein portion of these molecules. Consequently, oxygen and carbon dioxide do not compete for binding sites, and a hemoglobin molecule can transport both gases at the same time.

Carbon dioxide bonds loosely with hemoglobin amino groups, forming **carbaminohemoglobin** (kar-bam″ĭ-no-he″mo-glo′bin). This molecule decomposes readily in regions of low $Pco_2$, releasing its carbon dioxide. Transporting carbon dioxide this way is theoretically quite effective, but carbaminohemoglobin forms slowly. Only about 23% of the carbon dioxide that blood transports is in this form.

The most important carbon dioxide transport mechanism forms **bicarbonate ions** ($HCO_3^-$). Carbon dioxide reacts with water to form carbonic acid ($H_2CO_3$):

$$CO_2 + H_2O \longrightarrow H_2CO_3$$

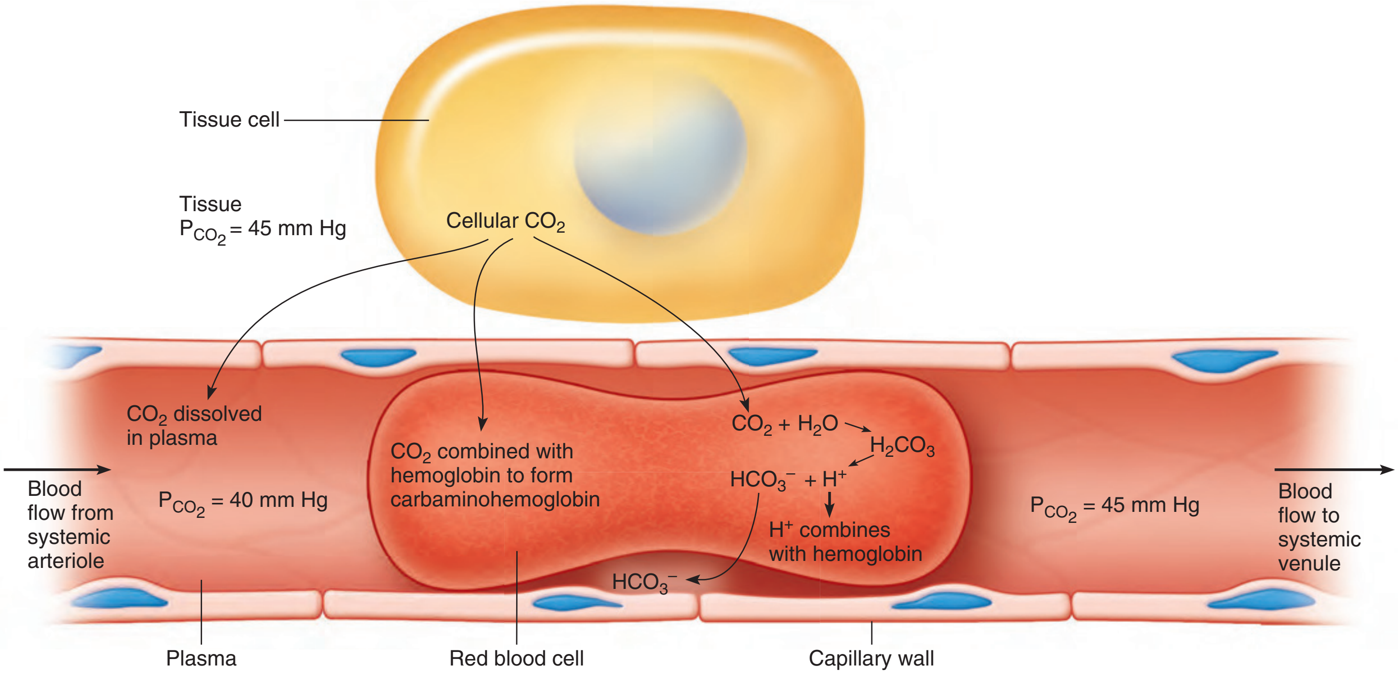

Tissue cell
Tissue
$P_{CO_2}$ = 45 mm Hg
Cellular $CO_2$
$CO_2$ dissolved in plasma
Blood flow from systemic arteriole
$P_{CO_2}$ = 40 mm Hg
$CO_2$ combined with hemoglobin to form carbaminohemoglobin
$CO_2 + H_2O$
$H_2CO_3$
$HCO_3^- + H^+$
$H^+$ combines with hemoglobin
$HCO_3^-$
$P_{CO_2}$ = 45 mm Hg
Blood flow to systemic venule
Plasma
Red blood cell
Capillary wall

**FIGURE 16.22** Carbon dioxide produced by cells is transported in the blood plasma in a dissolved state, bound to hemoglobin, or in the form of bicarbonate ions ($HCO_3^-$).

This reaction occurs slowly in plasma, but much of the carbon dioxide diffuses into red blood cells. These cells have the enzyme **carbonic anhydrase** (kar-bon′ik an-hi′drās), which greatly speeds the reaction between carbon dioxide and water. The resulting carbonic acid then dissociates, releasing hydrogen ions ($H^+$) and bicarbonate ions ($HCO_3^-$):

$$H_2CO_3 \longrightarrow H^+ + HCO_3^-$$

Most of the hydrogen ions bind hemoglobin molecules quickly, and thus do not accumulate and greatly change blood pH. The bicarbonate ions diffuse out of red blood cells and enter the plasma. Nearly 70% of the carbon dioxide that blood transports is in this form.

These reactions are reversible. When blood passes through the capillaries of the lungs, its dissolved carbon dioxide diffuses into alveoli in response to the relatively low $P_{CO_2}$ of alveolar air (fig. 16.23). At the same time, hydrogen ions and bicarbonate ions in red blood cells recombine to form carbonic acid, and under the influence of carbonic anhydrase, the carbonic acid quickly breaks down to yield carbon dioxide and water:

$$H^+ + HCO_3^- \longrightarrow H_2CO_3 \longrightarrow CO_2 + H_2O$$

Carbaminohemoglobin also releases its carbon dioxide, and carbon dioxide continues to diffuse out of the blood until the $P_{CO_2}$ of the blood and that of alveolar air are in equilibrium. (As is the case for oxygen, as long as breathing continues the $P_{CO_2}$ of alveolar air normally stays relatively constant.) Table 16.3 summarizes transport of blood gases.

**TABLE 16.3 Gases Transported in Blood**

| Gas | Reaction Involved | Substance Transported |
|---|---|---|
| Oxygen | 1–2% dissolves in plasma; 98–99% combines with iron atoms of hemoglobin molecules | Oxyhemoglobin |
| Carbon dioxide | About 7% dissolves in plasma | Carbon dioxide |
| | About 23% combines with amino groups of hemoglobin molecules | Carbaminohemoglobin |
| | About 70% reacts with water to form carbonic acid; the carbonic acid then dissociates to release hydrogen ions and bicarbonate ions | Bicarbonate ions |

The normal percentage of hemoglobin molecules that bind carbon monoxide (CO) in people who do not smoke is 2%. In people with CO poisoning, levels may exceed 20%. Carbon monoxide binds to hemoglobin in a way that prevents hemoglobin from delivering oxygen to the tissues. This can starve tissues of oxygen and causes chest pain, shortness of breath, fatigue, confusion, an irregular pulse, and abnormal heart rhythm.

## PRACTICE

33. Describe three forms in which blood can transport carbon dioxide from cells to the lungs.
34. How can hemoglobin carry oxygen and carbon dioxide at the same time?
35. How is carbon dioxide released from blood into the lungs?

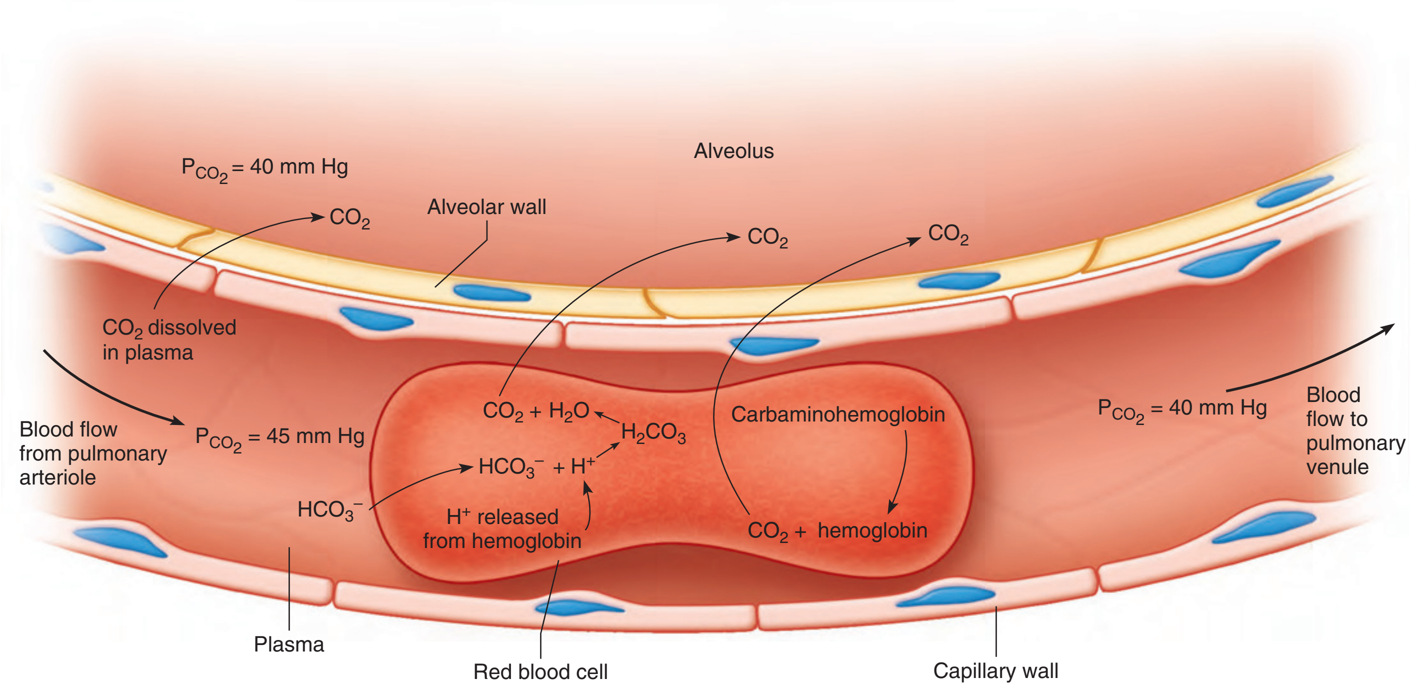
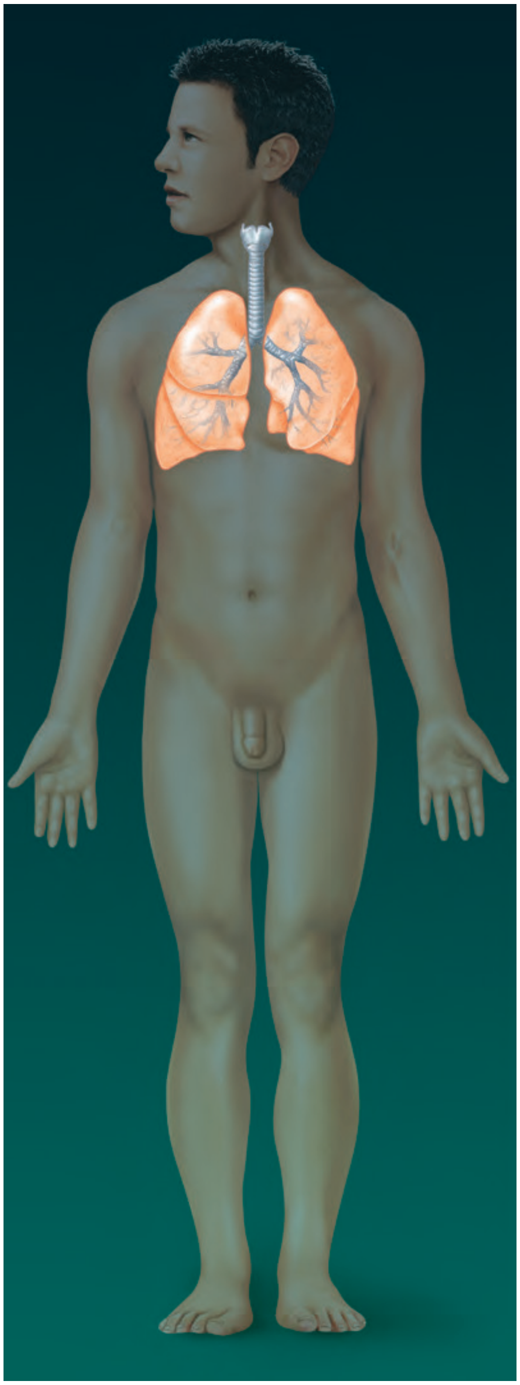


**FIGURE 16.23** In the lungs, carbon dioxide diffuses from the blood into the alveoli.

# Respiratory System

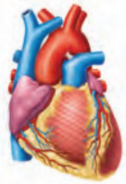


The respiratory system provides oxygen for the internal environment and excretes carbon dioxide.

## Integumentary System

Stimulation of skin receptors may alter respiratory rate.

## Cardiovascular System



As the heart pumps blood through the lungs, the lungs oxygenate the blood and excrete carbon dioxide.

## Skeletal System

Bones provide attachments for muscles involved in breathing.

## Lymphatic System

Cells of the immune system patrol the lungs and defend against infection.

## Muscular System

The respiratory system eliminates carbon dioxide produced by exercising muscles.

## Digestive System

The digestive system and respiratory system share openings to the outside.

## Nervous System

The brain controls the respiratory system.

## Urinary System

The kidneys and the respiratory system work together to maintain blood pH. The kidneys compensate for water lost through breathing.

## Endocrine System

Hormone-like substances control the production of red blood cells that transport oxygen and carbon dioxide.

## Reproductive System

Respiration increases during sexual activity. Fetal gas exchange begins before birth.

# Summary Outline

### 16.1 Introduction (p. 454)

*The respiratory system includes tubes that remove particles from incoming air and transport air to and from the lungs and the air sacs where gases are exchanged. Respiration is the entire process of gas exchange between the atmosphere and body cells.*

### 16.2 Organs and Associated Structures of the Respiratory System (p. 454)

*The respiratory system can be divided into two parts or tracts. The upper respiratory tract includes the nose, nasal cavity, paranasal sinuses, and pharynx; the lower respiratory tract includes the larynx, trachea, bronchial tree, and lungs.*

1. Nose
   a. Bone and cartilage support the nose.
   b. The nostrils are openings for air.
2. Nasal cavity
   a. Nasal conchae divide the nasal cavity into passageways and help increase the surface area of the mucous membrane.
   b. The mucous membrane filters, warms, and moistens incoming air.
   c. Ciliary action carries particles trapped in mucus to the pharynx, where they are swallowed.
3. Paranasal sinuses
   a. The paranasal sinuses are spaces in the bones of the skull that open into the nasal cavity.
   b. Mucous membrane lines the sinuses.
4. Pharynx
   a. The pharynx is behind the nasal cavity, oral cavity, and larynx.
   b. It is a passageway for air and food.
5. Larynx
   a. The larynx conducts air and helps prevent foreign objects from entering the trachea.
   b. It is composed of muscles and cartilages and is lined with mucous membrane.
   c. The larynx contains the vocal cords, which vibrate from side to side and produce sounds when air passes between them.
   d. The glottis and epiglottis help prevent foods and liquids from entering the trachea.
6. Trachea
   a. The trachea extends into the thoracic cavity anterior to the esophagus.
   b. It divides into right and left main bronchi.
7. Bronchial tree
   a. The bronchial tree consists of branched air passages that lead from the trachea to the air sacs.
   b. Alveoli are at the distal ends of the narrowest tubes, the alveolar ducts.
8. Lungs
   a. The mediastinum separates the left and right lungs, and the diaphragm and thoracic cage enclose them.
   b. The visceral pleura attaches to the surface of the lungs. The parietal pleura lines the thoracic cavity.
   c. Each lobe of the lungs is composed of alveoli, blood vessels, and supporting tissues.

### 16.3 Breathing Mechanism (p. 460)

*Changes in the size of the thoracic cavity accompany inspiration and expiration.*

1. Inspiration
   a. Atmospheric pressure provides the force that moves air into the lungs.
   b. Inspiration occurs when the pressure inside alveoli decreases.
   c. Pressure within alveoli decreases when the diaphragm moves downward and the thoracic cage moves upward and outward.
   d. Surface tension aids lung expansion.
2. Expiration
   a. Elastic recoil of tissues and surface tension within alveoli provide the forces of expiration.
   b. Thoracic and abdominal wall muscles aid expiration.
3. Respiratory air volumes and capacities
   a. One inspiration followed by one expiration is a respiratory cycle.
   b. The amount of air that moves in (or out) during a single respiratory cycle is the tidal volume.
   c. Additional air that can be inhaled is the inspiratory reserve volume. Additional air that can be exhaled is the expiratory reserve volume.
   d. Residual volume remains in the lungs after a maximal expiration.
   e. The vital capacity is the maximum amount of air a person can exhale after taking the deepest breath possible.
   f. The inspiratory capacity is the maximum volume of air a person can inhale following exhalation of the tidal volume.
   g. The functional residual capacity is the volume of air that remains in the lungs after a person exhales the tidal volume.
   h. The total lung capacity equals the vital capacity plus the residual volume.

### 16.4 Control of Breathing (p. 468)

*Normal breathing is rhythmic and involuntary.*

1. Respiratory areas
   a. The respiratory areas are in the brainstem and include parts of the medulla oblongata and pons.
   b. The medullary respiratory center includes two groups of neurons.
      (1) The ventral respiratory group gives rise to the basic rhythm of breathing.
      (2) The dorsal respiratory group stimulates inspiratory muscles.
   c. The pontine respiratory group may contribute to the rhythm of breathing by limiting inspiration.
2. Factors affecting breathing
   a. Chemicals, stretching of lung tissues, emotional state, and exercise affect breathing.
   b. Chemosensitive areas (central chemoreceptors) are associated with the respiratory center.
      (1) Blood levels of carbon dioxide and hydrogen ions influence the central chemoreceptors.
      (2) Stimulation of these receptors increases breathing rate.
   c. Peripheral chemoreceptors are in the walls of certain large arteries.
      (1) These chemoreceptors sense low oxygen levels.
      (2) When oxygen levels are low, breathing rate increases.
   d. Overstretching lung tissues triggers an inflation reflex.
      (1) This reflex shortens the duration of inspiratory movements.
      (2) The inflation reflex prevents overinflation of the lungs during forceful breathing.
   e. Hyperventilation decreases blood carbon dioxide levels, but *this may be dangerous when done before swimming underwater.*

### 16.5 Alveolar Gas Exchanges (p. 470)

*Gas exchange between air and blood occurs in alveoli.*

1. Alveoli
   Alveoli are tiny air sacs clustered at the distal ends of alveolar ducts.
2. Respiratory membrane
   a. This membrane consists of alveolar and capillary walls.
   b. Blood and alveolar air exchange gases across this membrane.
3. Diffusion across the respiratory membrane
   a. The partial pressure of a gas is proportional to the concentration of that gas in a mixture or the concentration dissolved in a liquid.

b. Gases diffuse from regions of higher partial pressure toward regions of lower partial pressure.
c. Carbon dioxide diffuses from blood into alveolar air. Oxygen diffuses from alveolar air into blood.

**16.6 Gas Transport (p. 472)**

*Blood transports gases between the lungs and cells.*

1. Oxygen transport
    a. Blood mainly transports oxygen in combination with hemoglobin molecules.
    b. The resulting oxyhemoglobin releases its oxygen in regions where the $P_{O_2}$ is low.
    c. More oxygen is released as the plasma $P_{CO_2}$ increases, as blood becomes more acidic, and as blood temperature increases.
2. Carbon dioxide transport
    a. Carbon dioxide may be carried dissolved in plasma, bound to hemoglobin, or as a bicarbonate ion.
    b. Most carbon dioxide is transported in the form of bicarbonate ions.
    c. The enzyme carbonic anhydrase speeds the reaction between carbon dioxide and water to form carbonic acid.
    d. Carbonic acid dissociates to release hydrogen ions and bicarbonate ions.

## CHAPTER ASSESSMENTS

### 16.1 Introduction

**1.** List the general functions of the respiratory system. (p. 454)

### 16.2 Organs and Associated Structures of the Respiratory System

**2.** Which one of the following is the beginning of the lower respiratory tract? (p. 454)
a. nostril
b. nasal cavity
c. pharynx
d. larynx

**3.** Explain how the nose and nasal cavity filter the incoming air. (p. 454)

**4.** Identify the locations of the major paranasal sinuses. (p. 455)

**5.** Match the following structures with their descriptions: (pp. 456–459)
(1) true vocal cords
(2) false vocal cords
(3) larynx
(4) visceral pleura
(5) alveoli

A. serous membrane on lungs
B. contains the vocal cords
C. vibrate to make sound
D. air sacs
E. muscular folds

**6.** Name and describe the locations of the larger cartilages of the larynx. (p. 456)

### 16.3 Breathing Mechanism

**7.** Explain how inspiration and expiration depend on pressure changes. (pp. 460–464)

**8.** Compare the muscles used in a resting inspiration with those in a forced inspiration. (p. 463)

**9.** Define *surface tension* and explain how it aids breathing. (p. 463)

**10.** Define *surfactant* and explain its function. (p. 463)

**11.** Compare the muscles used (if any) in a resting expiration with those in a forced expiration. (p. 464)

**12.** Distinguish between the vital capacity and the total lung capacity. (p. 467)

### 16.4 Control of Breathing

**13.** Describe the location of the respiratory areas and name the major components. (p. 468)

**14.** Chemosensitive areas in the medulla oblongata are most sensitive to levels of ______________. (p. 469)
a. nitrogen
b. oxygen
c. carbon dioxide
d. sodium

**15.** Describe the function of the chemoreceptors in the carotid and aortic bodies. (p. 469)

**16.** Describe the inflation reflex. (p. 469)

**17.** Hyperventilation is which one of the following? (p. 469)
a. any decrease in breathing
b. a decrease in breathing that brings in oxygen too slowly
c. an increase in breathing that eliminates carbon dioxide too quickly
d. any increase in breathing

### 16.5 Alveolar Gas Exchanges

**18.** Define *respiratory membrane* and indicate its function. (p. 470)

**19.** Explain the relationship between the partial pressure of a gas and diffusion of that gas. (p. 471)

**20.** Summarize the exchange of oxygen and carbon dioxide across the respiratory membrane. (p. 471)

### 16.6 Gas Transport

**21.** Identify how blood transports oxygen. (p. 472)

**22.** List three factors that increase the release of oxygen from hemoglobin. (p. 472)

**23.** Identify the three ways blood transports carbon dioxide. (p. 472)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOME 16.2

**1.** Why does breathing through the mouth dry out the throat?

### OUTCOMES 16.2, 16.3

**2.** It is below 0°F outside, but the dedicated runner bundles up and hits the road anyway. "You're crazy," shouts a neighbor. "Your lungs will freeze." Why is the well-meaning neighbor wrong?

### OUTCOMES 16.2, 16.3, 16.4

**3.** Emphysema reduces the lungs' capacity to recoil elastically. Which respiratory air volumes does emphysema affect?

### OUTCOMES 16.3, 16.4, 16.5

**4.** When a woman is very close to delivering a baby, she may hyperventilate. Breathing into a paper bag regulates her breathing. How does this action return her breathing to normal?

### OUTCOMES 16.3, 16.5, 16.6

**5.** Why were the finishing times of endurance events rather slow at the 1968 Olympics, held in 2,200-meter-high Mexico City?

### OUTCOMES 16.4, 16.5

**6.** If a person has stopped breathing and is receiving pulmonary resuscitation, would it be better to administer pure oxygen or a mixture of oxygen and carbon dioxide? Why?

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LEARN PRACTICE ASSESS

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**Connect Interactive Questions** Reinforce your knowledge using assigned interactive questions covering respiratory structures, the mechanics of breathing, and the process of gas transport to and from tissues.

**Connect Integrated Activity** Can you predict changes in respiration that will occur in various circumstances?

**LearnSmart** Discover which chapter concepts you have mastered and which require more attention. This adaptive learning tool is personalized, proven, and preferred.

**Anatomy & Physiology Revealed** Go more in depth into the human body by exploring the upper respiratory tract and lower respiratory tract structures. Also view animations on the process of breathing.

# 17

# Urinary System

*Spinach tainted with Escherichia coli strain 0157:H7 may cause food poisoning that can lead to the health complication of hemolytic uremic syndrome.*

**H**emolytic uremic syndrome. People became infected with *Escherichia coli* strain 0157:H7 from eating raw spinach, mostly in sandwiches or salads. Two-year-old Kyle had consumed spinach that his mother had mixed into a fruit drink. When the story was reported in the news, many people commented on the irony of becoming ill from eating or drinking such a healthy food, but a few years later another outbreak of *E. coli*-related food poisoning occurred, traced this time to tainted, raw, chocolate chip cookie dough.

*E. coli* is a common bacterium that can cause severe illness when it produces a poison called shigatoxin. The illness begins with sharp abdominal pain and bloody diarrhea. Intensifying pain sends many victims to hospitals. For about 10% of them, the condition worsens to hemolytic uremic syndrome (HUS), which develops as the bloodstream transports the toxin to the kidneys, where the toxin destroys the microscopic capillaries that normally prevent proteins and blood cells from being excreted. With the capillaries compromised, proteins and blood cells, as well as damaged kidney cells, appear in the urine. HUS causes acute kidney failure. Blood forms clots around the sites of the damaged capillaries. Usually after weeks of hospitalization the person recovers, but in some cases, the kidney damage may be permanent. For a few people, such as two-year-old Kyle, HUS is deadly.

*E. coli* outbreaks have occurred in a variety of circumstances involving exposure to bacteria-laden manure—such as eating undercooked beef, drinking unpasteurized apple cider, or picking up bacteria from petting farm animals. Epidemiologists used DNA tests to trace the spinach that sickened Kyle and others in twenty-two states to a single facility in California where the vegetable was contaminated with runoff from a nearby cattle ranch. But sometimes old-fashioned sleuthing solves the mystery. Epidemiologists traced the source of infection in twenty-six people who developed HUS in Germany to contaminated sprouts served at a single restaurant.

## LEARNING OUTCOMES

***After studying this chapter, you should be able to do the following:***

### 17.1 Introduction

1. List the general functions of the organs of the urinary system. (p. 480)

### 17.2 Kidneys

2. Describe the locations and structure of the kidneys. (p. 480)
3. List the functions of the kidneys. (p. 482)
4. Trace the pathway of blood through the major vessels in a kidney. (p. 482)
5. Describe a nephron, and explain the functions of its major parts. (p. 483)

### 17.3 Urine Formation

6. Explain how glomerular filtrate is produced, and describe its composition. (p. 487)
7. Explain the factors that affect the rate of glomerular filtration and how this rate is regulated. (pp. 488–489)
8. Discuss the role of tubular reabsorption in urine formation. (pp. 490–492)
9. Define *tubular secretion,* and explain its role in urine formation. (p. 492)

### 17.4 Urine Elimination

10. Describe the structure of the ureters, urinary bladder, and urethra. (pp. 495–497)
11. Explain the process and control of micturition. (p. 496)

Anatomy & Physiology REVEALED apREVEALED.com **Module 13** Urinary System

LEARN PRACTICE ASSESS

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**calyc-** [small cup] major *calyc*es: Cuplike divisions of the renal pelvis.

**cort-** [covering] renal *cort*ex: Shell of tissues surrounding the inner kidney.

**detrus-** [to force away] *detrus*or muscle: Muscle within the bladder wall that expels urine.

**glom-** [little ball] *glom*erulus: Cluster of capillaries within a renal corpuscle.

**mict-** [to pass urine] *mict*urition: Process of expelling urine from the urinary bladder.

**nephr-** [pertaining to the kidney] *nephr*on: Functional unit of a kidney.

**papill-** [nipple] renal *papill*ae: Small elevations that project into a renal calyx.

**trigon-** [triangle] *trigon*e: Triangular area on the internal floor of the urinary bladder.

---

## 17.1 | Introduction

Cells produce a variety of wastes that are toxic if they accumulate. Body fluids, such as blood and lymph, carry wastes from the tissues that produce them, while other structures remove wastes from the blood and transport them to the outside. The respiratory system removes carbon dioxide from the blood, and the *urinary system* removes certain salts and nitrogenous wastes. The urinary system also helps maintain the normal concentrations of water and electrolytes in body fluids, regulates the pH and volume of body fluids, and helps control red blood cell production and blood pressure.

The urinary system consists of a pair of kidneys, which remove substances from the blood, form urine, and help regulate certain metabolic processes; a pair of tubular ureters, which transport urine from the kidneys; a saclike urinary bladder, which stores urine; and a tubular urethra, which conveys urine to the outside of the body. Figure 17.1 and reference plate 6 (p. 37) show these organs.

## 17.2 | Kidneys

A **kidney** is a reddish-brown, bean-shaped organ with a smooth surface. An adult kidney is about 12 centimeters long, 6 centimeters wide, and 3 centimeters thick, and is enclosed in a tough, fibrous capsule (fig. 17.2).

### Location of the Kidneys

The kidneys lie on either side of the vertebral column in a depression high on the posterior wall of the abdominal cavity. The upper and lower borders of the

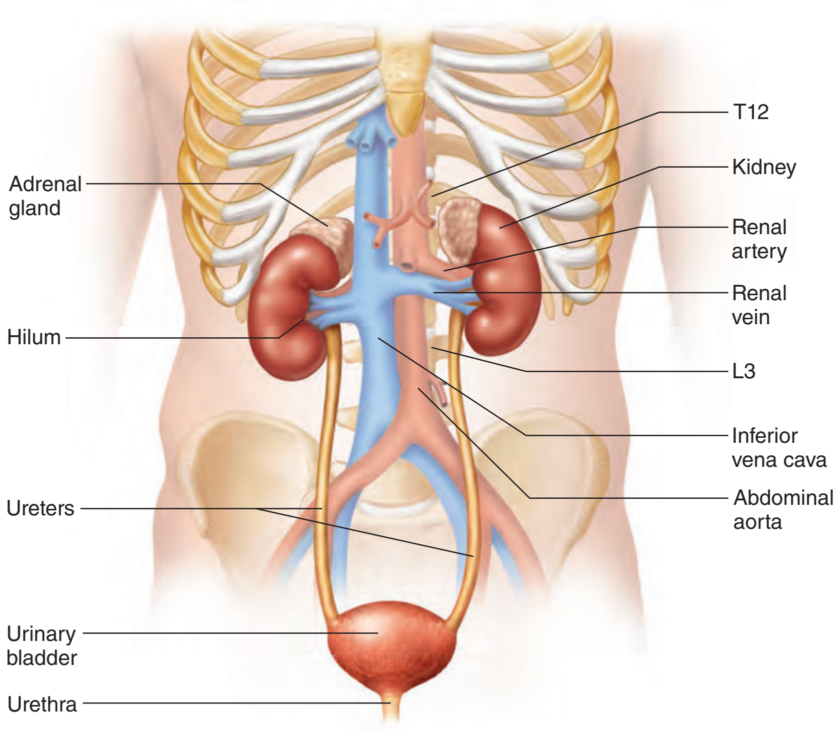


**FIGURE 17.1** APR The urinary system includes the kidneys, ureters, urinary bladder, and urethra. Note the relationship of these structures to the major blood vessels.

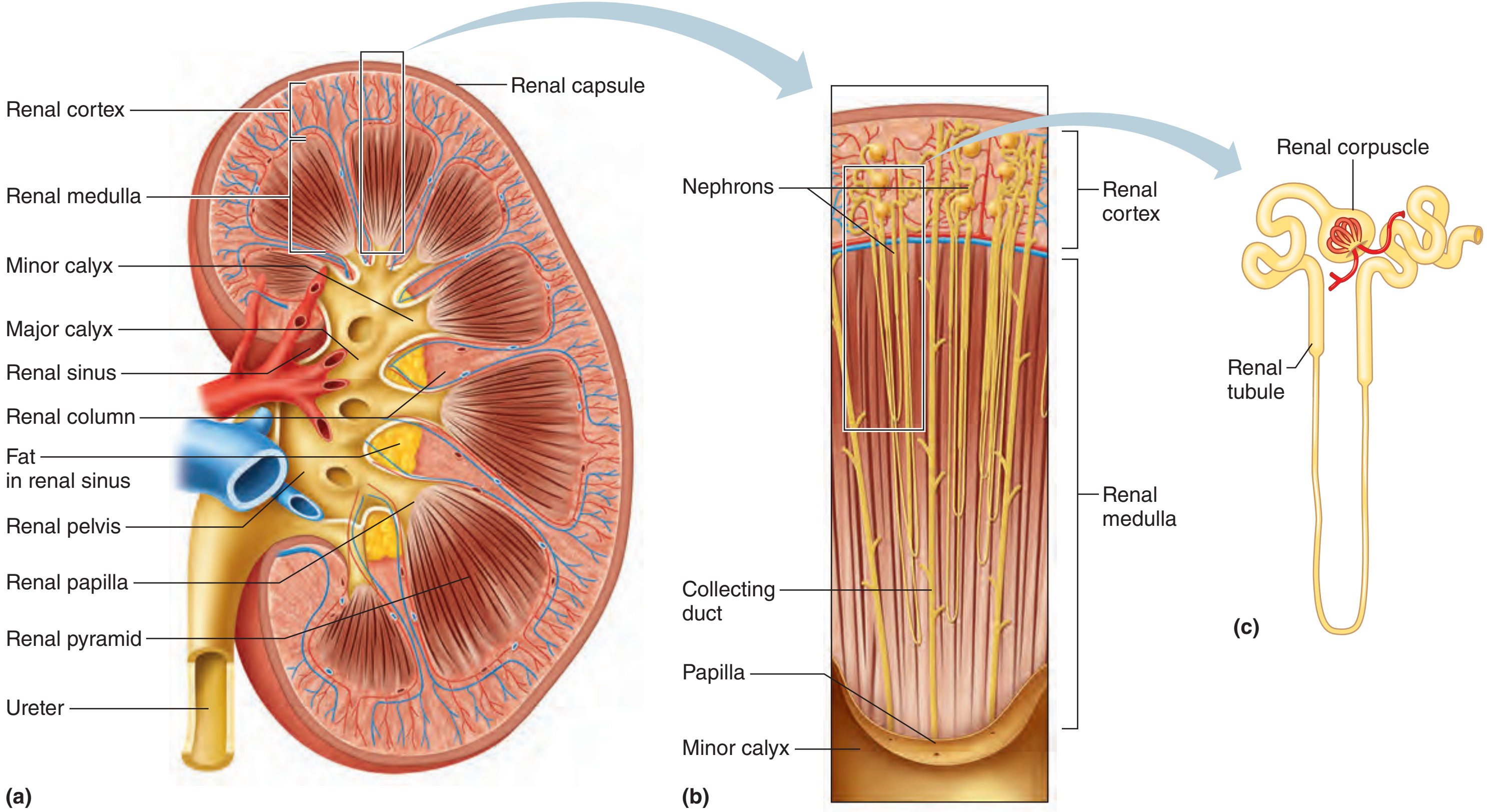

Renal cortex
Renal medulla
Minor calyx
Major calyx
Renal sinus
Renal column
Fat in renal sinus
Renal pelvis
Renal papilla
Renal pyramid
Ureter
Renal capsule
(a)
Nephrons
Collecting duct
Papilla
Minor calyx
Renal cortex
Renal medulla
(b)
Renal corpuscle
Renal tubule
(c)

**FIGURE 17.2** APR The kidney. (**a**) Longitudinal section of a kidney. (**b**) A renal pyramid containing nephrons. (**c**) A single nephron.

kidneys are generally at the levels of the twelfth thoracic and third lumbar vertebrae, respectively. In most individuals the left kidney is 1.5–2.0 centimeters higher than the right one.

The kidneys are positioned **retroperitoneally** (ret″ro-per″ĭ-to-ne′alē), which means they are behind the parietal peritoneum and against the deep muscles of the back. Connective tissue and masses of adipose tissue surround the kidneys and hold them in position (see fig. 1.12, p. 20).

## Kidney Structure

The lateral surface of each kidney is convex, but its medial side is deeply concave. The resulting medial depression leads into a hollow chamber called the **renal sinus.** The entrance to this sinus is the *hilum,* and through it pass blood vessels, nerves, lymphatic vessels, and the ureter (see fig. 17.1).

The superior end of the ureter expands to form a funnel-shaped sac called the **renal pelvis** (re′nal pel′vis) inside the renal sinus. The pelvis is divided into two or three tubes, called *major calyces* (singular, *calyx*), and these in turn are divided into several *minor calyces* (fig. 17.2*a*).

### CAREER CORNER

### Dialysis Technician

The eighty-three-year-old woman's kidneys have been slowly failing for several years. Now, with 90% of her nephrons damaged, she requires hemodialysis to cleanse her blood of toxins and wastes and remove excess fluid. A nephrologist has prescribed dialysis three times a week, for three to four hours per session, to treat her chronic kidney disease.

A dialysis technician performs the tasks of hemodialysis, including:

- Setting up, cleaning, sterilizing, and using the dialysis machine.
- Preparing dialysis solutions.
- Monitoring and documenting vital signs.
- Preparing and administering medication.

Dialysis technicians work in hospitals and dialysis centers, as well as assist patients performing peritoneal dialysis in their homes. Training programs typically take two semesters, leading to a written exam for certification and national licensure. Students learn anatomy and physiology, nutrition, transplantation, pharmacology, health information management, medical terminology, and clinical skills related to performing dialysis.

A series of small elevations called *renal papillae* project into the renal sinus from its wall. Tiny openings that lead into a minor calyx pierce each projection.

Each kidney has two distinct regions—an inner medulla and an outer cortex. The **renal medulla** (re′nal mĕ-dul′ah) is composed of conical masses of tissue called *renal pyramids* and appears striated. The **renal cortex** (re′nal kor′teks), which appears granular, forms a shell around the medulla and dips into the medulla between renal pyramids, forming *renal columns.* The granular appearance of the cortex and the striations of the medulla are due to the organization of the tiny renal corpuscles and renal tubules associated with the **nephrons** (nef′ronz), the parts of the kidney that produce urine (fig. 17.2*b, c*).

## PRACTICE

1. Where are the kidneys located?
2. Describe kidney structure.
3. Name the kidney's functional unit.

## Kidney Functions

The primary function of the kidneys is to help maintain homeostasis by regulating the composition (including pH) and the volume of the extracellular fluid. They accomplish this by removing metabolic wastes from the blood and combining them with excess water and electrolytes to form urine, which they then excrete.

The kidneys have several other important functions:

- Secreting the hormone erythropoietin (see chapter 12, p. 329) to help control the rate of red blood cell production.
- Playing a role in the activation of vitamin D.
- Helping to maintain blood volume and blood pressure by secreting the enzyme renin.

## Renal Blood Vessels

The **renal arteries,** which arise from the abdominal aorta, supply blood to the kidneys. These arteries transport a large volume of blood. When a person is at rest, the renal arteries usually carry 15–30% of the total cardiac output into the kidneys.

A renal artery enters a kidney through the hilum and gives off several branches, called *interlobar arteries,* which pass between the renal pyramids. At the junction between the medulla and the cortex, the interlobar arteries branch, forming a series of incomplete arches, the *arcuate arteries,* which in turn give rise to *cortical radiate arteries (interlobular arteries).* The final branches of the cortical radiate arteries, called **afferent arterioles** (af′er-ent ar-te′re-ōlz), lead to the nephrons (figs. 17.3 and 17.4).

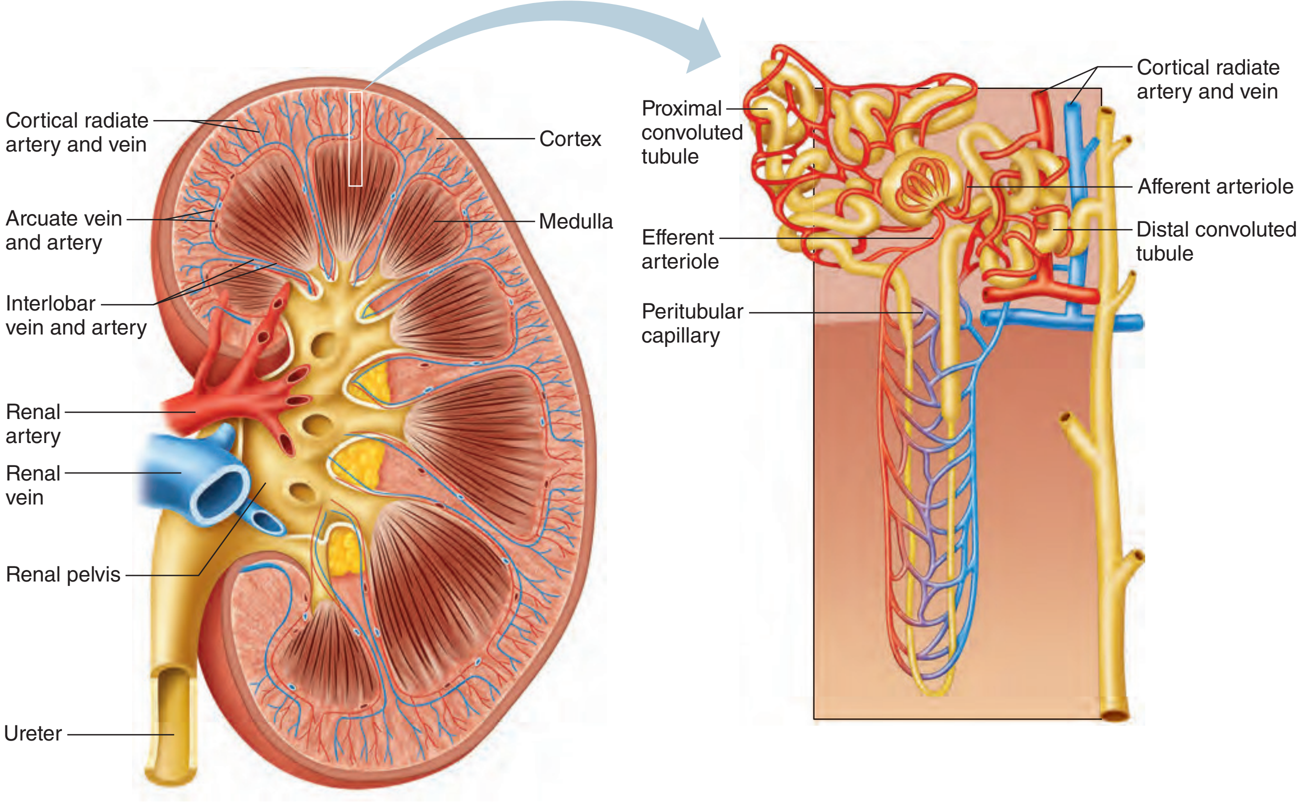

Cortical radiate artery and vein
Arcuate vein and artery
Interlobar vein and artery
Renal artery
Renal vein
Renal pelvis
Ureter
Cortex
Medulla
Proximal convoluted tubule
Efferent arteriole
Peritubular capillary
Cortical radiate artery and vein
Afferent arteriole
Distal convoluted tubule

**FIGURE 17.3** APR Main branches of the renal artery and renal vein.

Venous blood returns through a series of vessels that correspond generally to arterial pathways. The **renal vein** then joins the inferior vena cava as it courses through the abdominal cavity (see fig. 17.1).

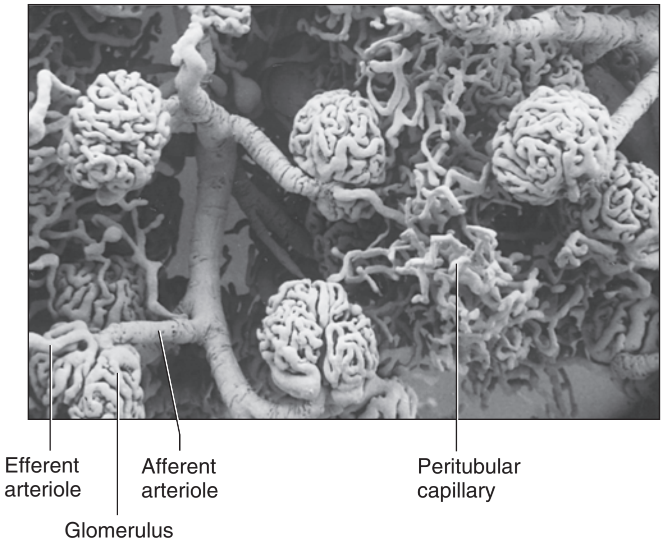


**FIGURE 17.4** Scanning electron micrograph of a cast of the renal blood vessels associated with glomeruli (200×). From *Tissues and Organs: A Text-Atlas of Scanning Electron Microscopy,* by R. G. Kessel and R. H. Kardon, © 1979 W. H. Freeman and Company, all rights reserved.

A kidney transplant can help patients with end-stage renal disease. This procedure requires a kidney from a living or recently deceased donor whose cell surfaces are antigenically similar (histocompatible) to those of the recipient. After removing the diseased kidney, a surgeon places the donor kidney into the depression on the medial surface of the right or left ilium (iliac fossa). The surgeon then connects the renal artery and vein of the donor kidney to the recipient's iliac artery and vein, respectively, and the ureter of the donor kidney to the recipient's urinary bladder.

## Nephrons

### *Nephron Structure*

Certain organs can be broken down into subunits, each of which performs the functions of the organ as a whole. In the kidney, the nephrons are such functional units.

A kidney contains about one million nephrons. Each nephron consists of a **renal corpuscle** (re′nal kor′pusl) and a **renal tubule** (re′nal tu′būl) (see fig. 17.2*c*). Fluid flows through renal tubules on its way out of the body.

A renal corpuscle is composed of a tangled cluster of blood capillaries called a **glomerulus** (glo-mer′u-lus). Glomerular capillaries filter fluid, which is the first step in urine formation. A thin-walled, saclike structure called a **glomerular capsule** (glo-mer′u-lar kap′sūl) surrounds the glomerulus (figs. 17.5*a*, 17.6*a* and *b*, 17.7).

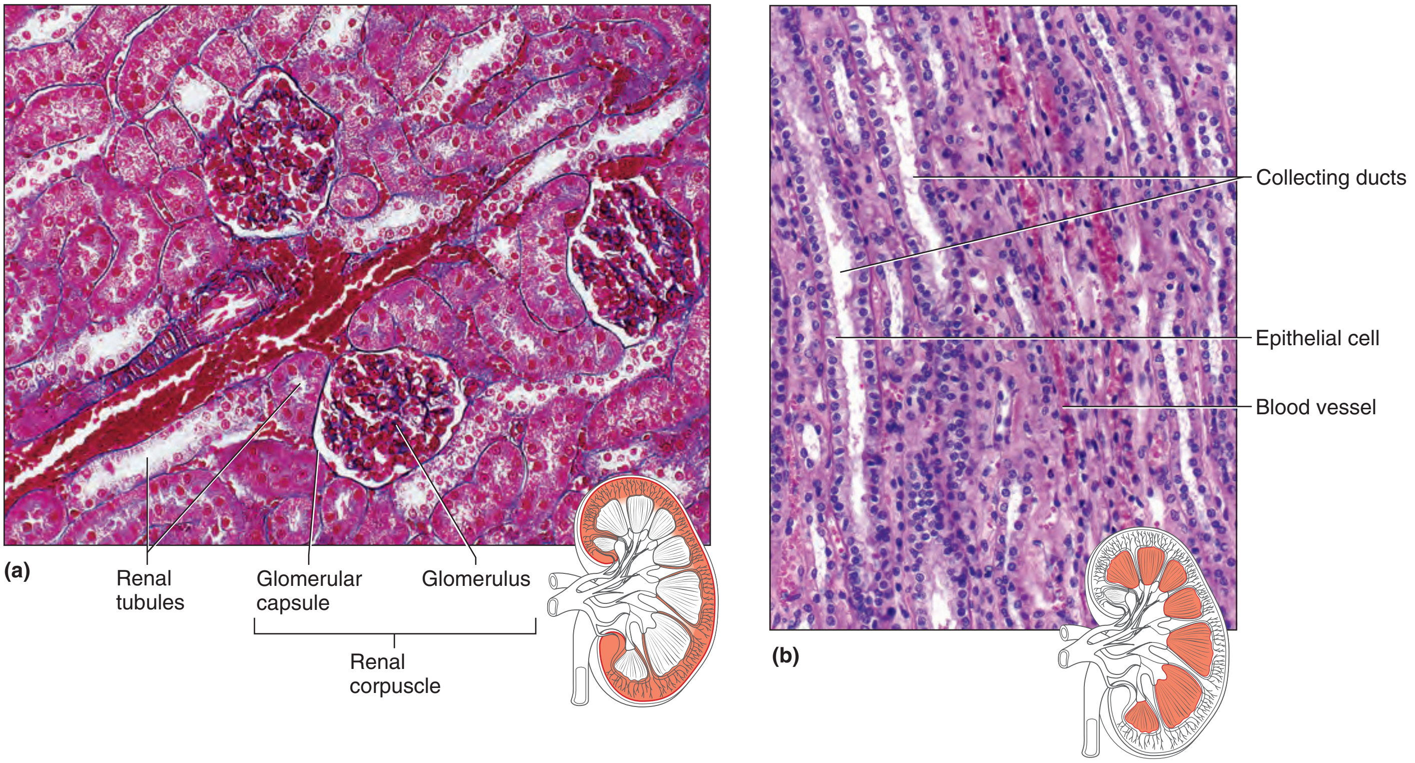


**FIGURE 17.5** APR Microscopic view of the kidney. (**a**) Light micrograph of a section of the human renal cortex (220×). (**b**) Light micrograph of the renal medulla (80×).

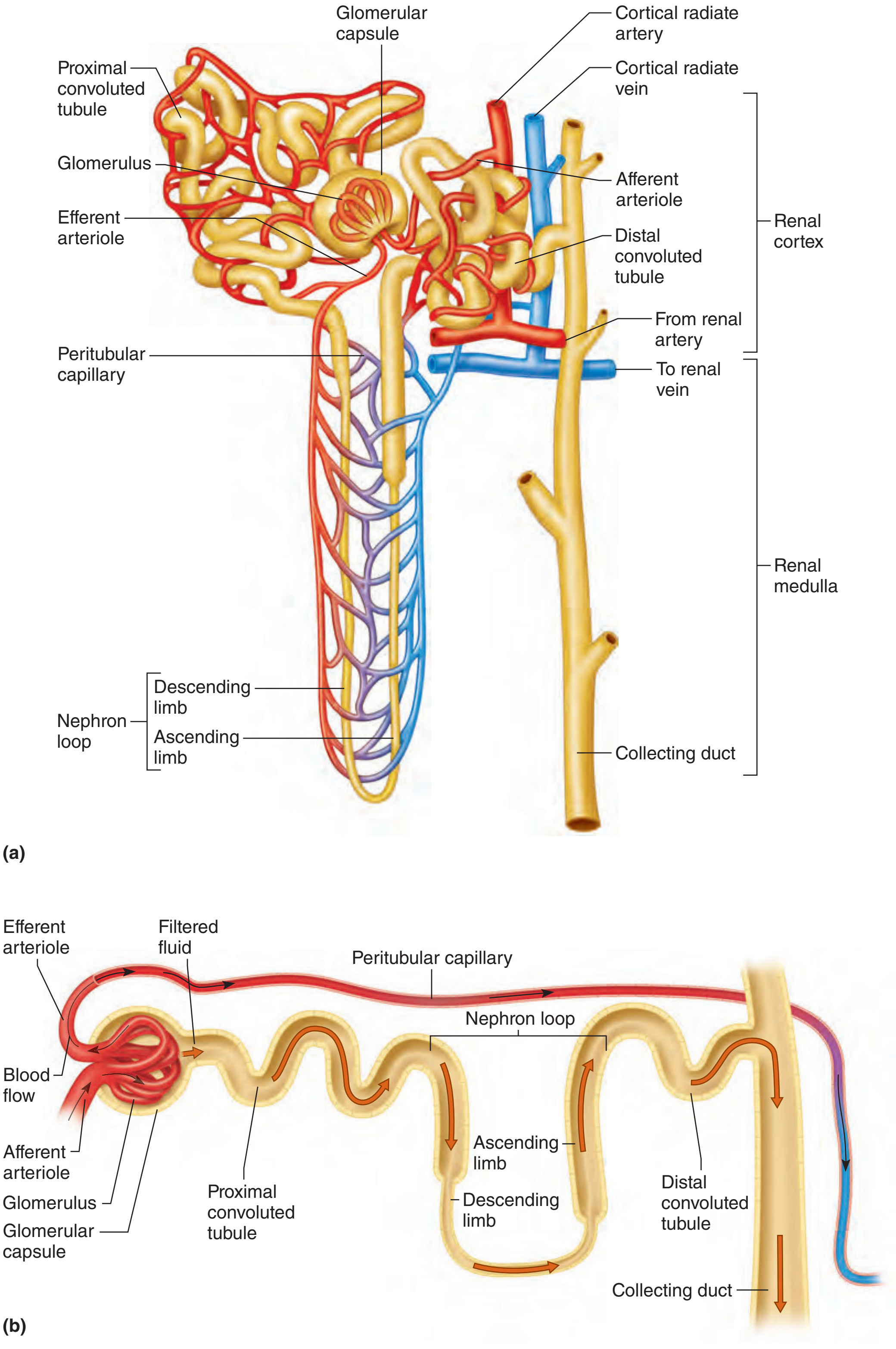

Glomerular capsule
Cortical radiate artery
Cortical radiate vein
Proximal convoluted tubule
Glomerulus
Efferent arteriole
Afferent arteriole
Distal convoluted tubule
Renal cortex
From renal artery
To renal vein
Peritubular capillary
Renal medulla
Nephron loop
Descending limb
Ascending limb
Collecting duct
(a)
Efferent arteriole
Filtered fluid
Peritubular capillary
Nephron loop
Blood flow
Afferent arteriole
Glomerulus
Glomerular capsule
Proximal convoluted tubule
Ascending limb
Descending limb
Distal convoluted tubule
Collecting duct
(b)

**FIGURE 17.6** APR A nephron. (**a**) Structure of a nephron and associated blood vessels. (**b**) Schematic representation of a nephron and the blood vessels associated with it.

The glomerular capsule, which is an expansion at the proximal end of a renal tubule, receives the fluid filtered at the glomerulus. The renal tubule leads away from the glomerular capsule and coils into a part of the nephron called the *proximal convoluted tubule.*

The proximal convoluted tubule dips toward the renal pelvis, where it becomes the *descending limb of the nephron loop* (loop of Henle). The tubule then curves back toward its renal corpuscle and forms the *ascending limb of the nephron loop.* The ascending limb returns to the region of the renal corpuscle, where it coils tightly again and is called the *distal convoluted tubule.*

Distal convoluted tubules from several nephrons merge in the renal cortex to form a *collecting duct* (technically not part of any one nephron), which in turn passes into the renal medulla and enlarges as other distal convoluted tubules join it. The resulting tube empties into a minor calyx through an opening in a renal papilla. Figure 17.6*a* and *b* summarize the structure of a nephron and its associated blood vessels. Figure 17.7 summarizes the various structures of the urinary system and the sequence in which they function.

### PRACTICE

4. List the general functions of the kidneys.
5. Trace the blood supply to the nephron.
6. Name the parts of a nephron.

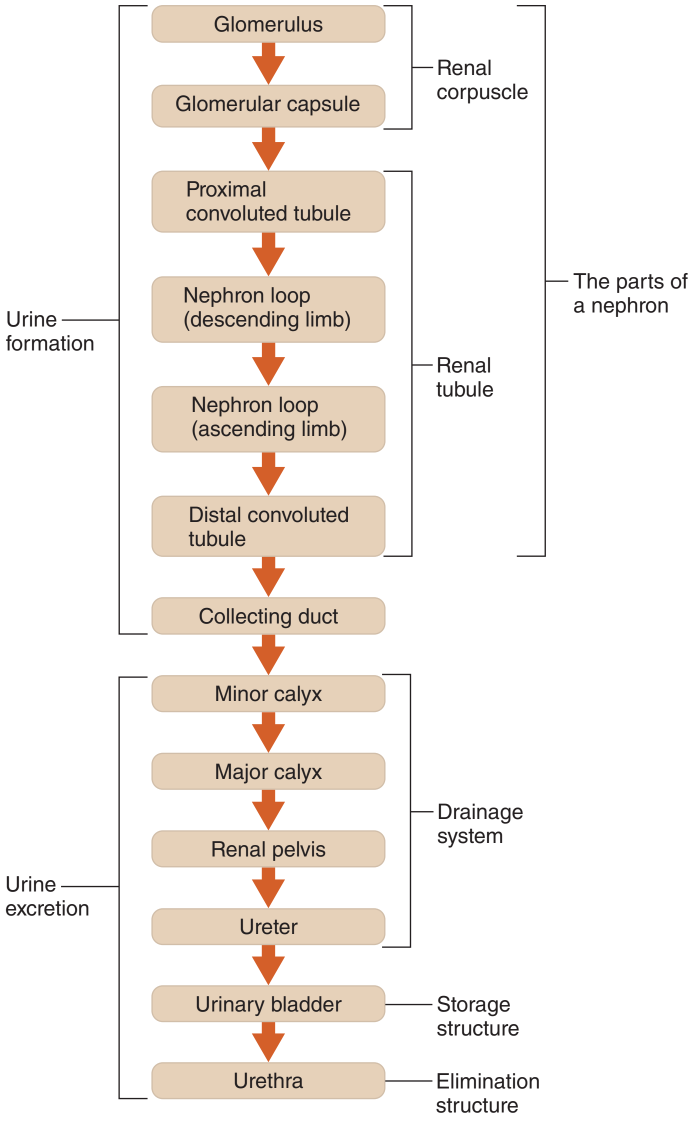

Glomerulus
Glomerular capsule
Renal corpuscle
Proximal convoluted tubule
Nephron loop (descending limb)
Nephron loop (ascending limb)
Distal convoluted tubule
Renal tubule
The parts of a nephron
Urine formation
Collecting duct
Minor calyx
Major calyx
Renal pelvis
Ureter
Drainage system
Urine excretion
Urinary bladder
Storage structure
Urethra
Elimination structure

**FIGURE 17.7** Structures associated with urine formation and excretion.

### *Blood Supply of a Nephron*

The cluster of capillaries that forms a glomerulus arises from an afferent arteriole. After passing through the glomerular capillaries, blood (minus any filtered fluid) enters an **efferent arteriole** (ef′er-ent ar-te′re-ōl) (see figs. 17.4 and 17.6*a* and *b*). This is different from entering a venule, the usual circulatory route.

The efferent arteriole branches into a complex, freely interconnecting network of capillaries, called the **peritubular capillary** (per″ĭ-tu′bu-lar kap′ĭ-ler″e) **system,** that surrounds the renal tubule (see figs. 17.4 and 17.6*a* and *b*). Blood in the peritubular capillary system has passed through two arterioles and is under relatively low pressure even for a capillary. After flowing through the peritubular capillary network, the blood enters the venous system of the kidney.

### *Juxtaglomerular Apparatus*

Near its end, the ascending limb of the nephron loop passes between and contacts the afferent and efferent arterioles. At the point of contact, the epithelial cells of the ascending limb are quite narrow and densely packed, forming a structure called the *macula densa.*

In the walls of the arterioles near their attachments to the glomerulus are large smooth muscle cells called *juxtaglomerular cells.* With cells of the macula densa, they constitute the **juxtaglomerular apparatus** (juks″tah-glo-mer′u-lar ap″ah-ra′tus) (fig. 17.8). Its role in the control of renin secretion is described on page 489.

### PRACTICE

7. Describe the system of blood vessels associated with a nephron.
8. Which structures form the juxtaglomerular apparatus?

## 17.3 | Urine Formation

The process of urine formation begins when the glomerular capillaries filter plasma, a process called **glomerular filtration.** Recall from chapter 13 (p. 367) that the force of blood pressure promotes filtration at capillaries throughout the body, but most of this fluid is reabsorbed into the bloodstream by the colloid osmotic pressure of the plasma (fig. 17.9*a*). Nephrons take filtration and reabsorption to another level, using two capillary beds working in series, the glomerulus and the peritubular capillaries. The first capillary bed, the glomerulus, is specialized only to filter. Instead of forming interstitial fluid, the filtered fluid (filtrate) moves into the renal tubule as *tubular fluid*, where much of it will become urine (fig. 17.9*b*).

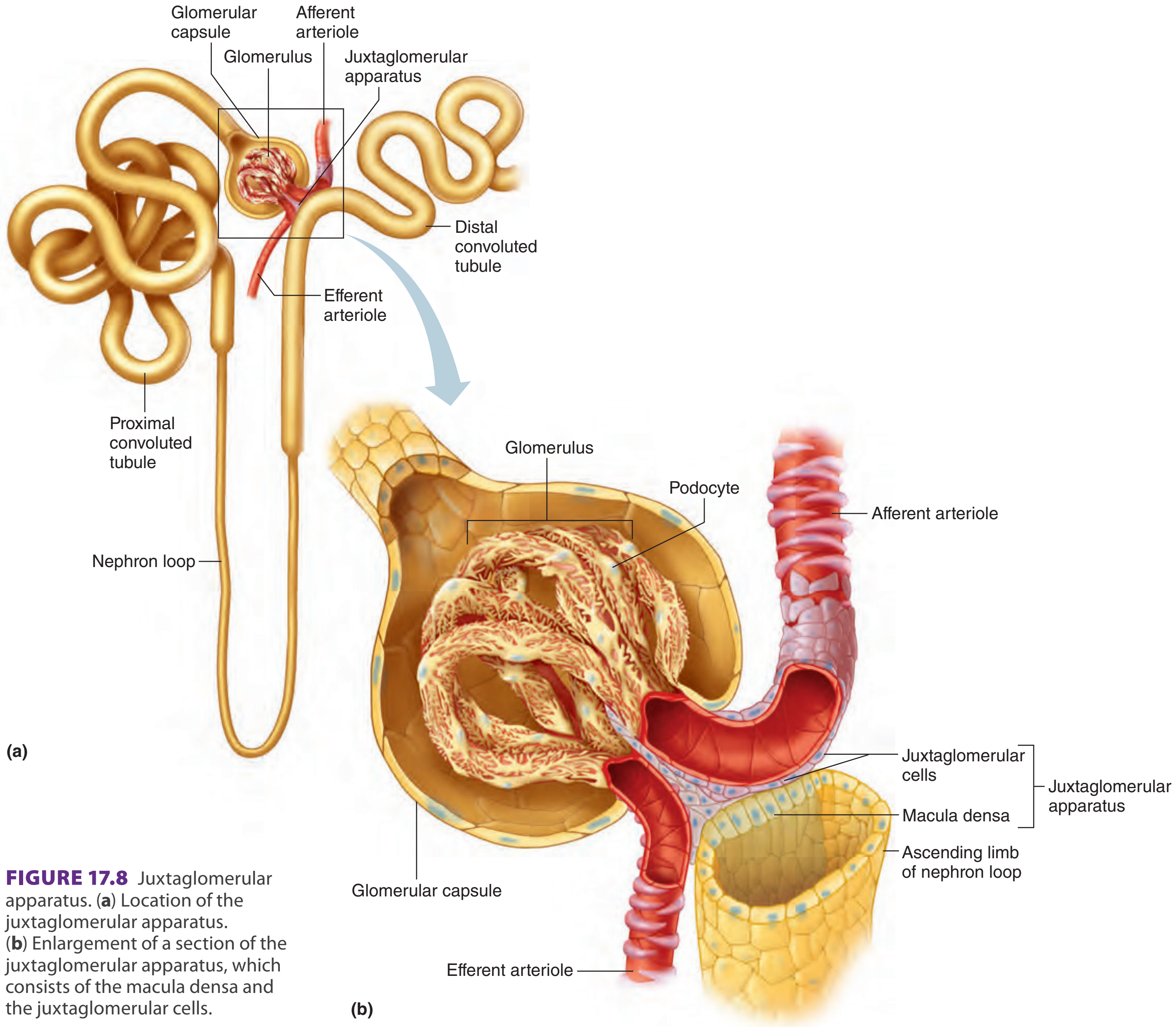

Glomerular capsule
Afferent arteriole
Glomerulus
Juxtaglomerular apparatus
Distal convoluted tubule
Efferent arteriole
Proximal convoluted tubule
Nephron loop
(a)
Glomerulus
Podocyte
Afferent arteriole
Juxtaglomerular cells
Juxtaglomerular apparatus
Macula densa
Ascending limb of nephron loop
Glomerular capsule
Efferent arteriole
(b)

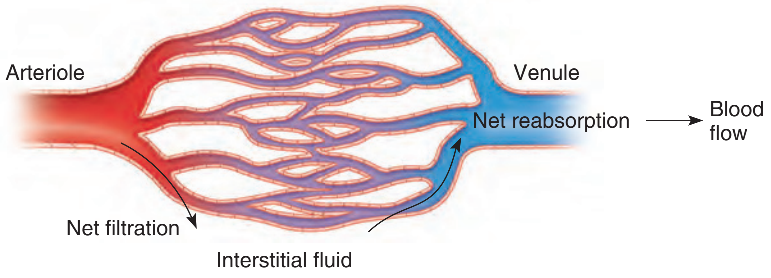
**FIGURE 17.8** Juxtaglomerular apparatus. (**a**) Location of the juxtaglomerular apparatus. (**b**) Enlargement of a section of the juxtaglomerular apparatus, which consists of the macula densa and the juxtaglomerular cells.

Glomerular filtration produces about 180 liters of fluid, more than four times the total body water, every 24 hours. This is many times more than the volume filtered at capillaries elsewhere in the body. However, 180 liters is not your daily urine output! Glomerular filtration could not continue for very long unless most of this filtered fluid were returned to the bloodstream. This is accomplished by **tubular reabsorption** (tu′bu-lar re-absorp′shun), which moves substances from the tubular fluid back into the blood within the peritubular capillaries. In contrast, **tubular secretion** (tu′bu-lar se-kre′shun), the reverse process, moves substances from the blood within the peritubular capillary system into the renal tubule (fig. 17.9*b*).

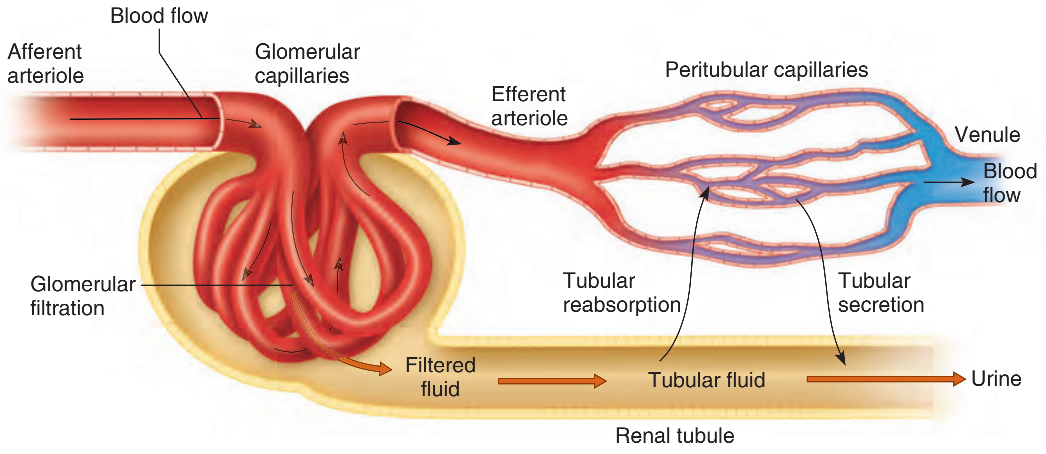
Tubular reabsorption and tubular secretion join glomerular filtration in forming urine. In tubular reabsorption, the kidney selectively reclaims just the right amounts of substances, such as water, electrolytes, and glucose, that the body requires. Waste and substances that are in excess exit the body. In tubular secretion, some substances that the body must excrete, such as hydrogen ions and certain toxins, are removed faster than through filtration alone.

The final product of these three processes—glomerular filtration, tubular reabsorption, and tubular secretion—is **urine.** The following relationship determines the amount of any given substance excreted in the urine:

Amount filtered at the glomerulus
– Amount reabsorbed by the tubule
+ Amount secreted by the tubule
= Amount excreted in the urine


Arteriole
Venule
Net reabsorption
Blood flow
Net filtration
Interstitial fluid

**(a)** In most systemic capillaries, filtration predominates at the arteriolar end and osmotic reabsorption predominates at the venular end.


Blood flow
Afferent arteriole
Glomerular capillaries
Efferent arteriole
Peritubular capillaries
Venule
Blood flow
Glomerular filtration
Tubular reabsorption
Tubular secretion
Filtered fluid
Tubular fluid
Urine
Renal tubule

**(b)** In the kidneys, the glomerular capillaries are specialized for filtration. The renal tubule is specialized to control movements of substances back into the blood of the peritubular capillaries (tubular reabsorption) or from the blood into the renal tubule (tubular secretion).

**FIGURE 17.9** Compared to most capillary beds in the (**a**) systemic circulation, those in the (**b**) kidneys are highly specialized for filtration.

As the kidneys selectively excrete waste products and excess materials in the urine, they maintain the composition of the internal environment, thereby contributing to homeostasis.

## Glomerular Filtration

Urine formation begins when water and certain dissolved substances are filtered out of glomerular capillaries and into glomerular capsules (fig. 17.10*a*). This filtration is similar to filtration at the arteriolar ends of other capillaries. However, many tiny openings (fenestrae) in glomerular capillary walls make glomerular capillaries much more permeable than capillaries in other tissues, even though cells called *podocytes* cover these capillaries and help make them impermeable to plasma proteins (figs. 17.8*b* and 17.10*a*).

The glomerular capsule receives the resulting **glomerular filtrate,** which is similar in composition to the filtrate that becomes tissue fluid elsewhere in the body. That is, glomerular filtrate is mostly water and the same components as blood plasma, except for most protein molecules, which are too big to be filtered. Table 17.1 shows the relative concentrations of some substances in plasma, glomerular filtrate, and urine.

**TABLE 17.1** **Relative Concentrations of Substances in the Plasma, Glomerular Filtrate, and Urine**

CONCENTRATIONS (mEq/L)

| Substance | Plasma | Glomerular Filtrate | Urine |
|---|---|---|---|
| Sodium ($Na^+$) | 142 | 142 | 128 |
| Potassium ($K^+$) | 5 | 5 | 60 |
| Calcium ($Ca^{+2}$) | 4 | 4 | 5 |
| Magnesium ($Mg^{+2}$) | 3 | 3 | 15 |
| Chloride ($Cl^-$) | 103 | 103 | 134 |
| Bicarbonate ($HCO_3^-$) | 27 | 27 | 14 |
| Sulfate ($SO_4^{-2}$) | 1 | 1 | 33 |
| Phosphate ($PO_4^{-3}$) | 4 | 4 | 40 |

CONCENTRATIONS (mg/100 mL)

| Substance | Plasma | Glomerular Filtrate | Urine |
|---|---|---|---|
| Glucose | 100 | 100 | 0 |
| Urea | 26 | 26 | 1,820 |
| Uric acid | 4 | 4 | 53 |

Note: mEq/L = milliequivalents per liter.

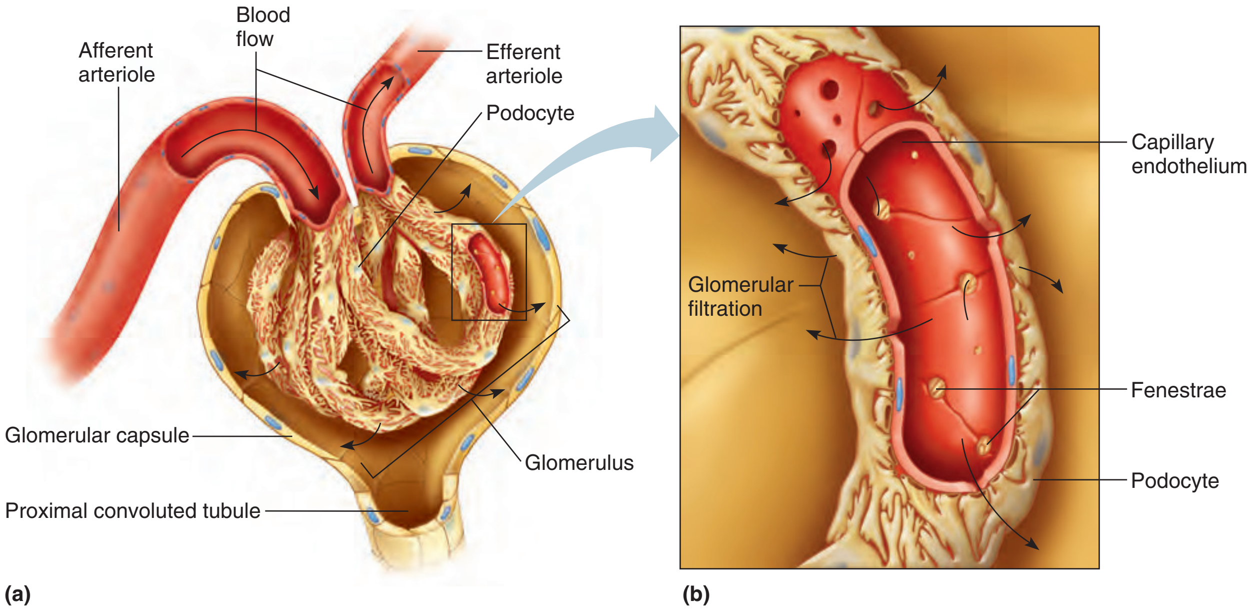


**FIGURE 17.10** Glomerular filtration. (**a**) The first step in urine formation is filtration of substances out of glomerular capillaries and into the glomerular capsule. (**b**) Glomerular filtrate passes through the fenestrae of the capillary endothelium.

**Q** *Vasoconstriction of which blood vessel in this figure would decrease glomerular filtration?*
**Answer can be found in Appendix F on page 582.**

## Filtration Pressure

The main force that moves substances by filtration through the glomerular capillary wall, as in other capillaries, is the hydrostatic pressure of the blood inside. The afferent arterioles have diameters larger than arterioles elsewhere in the body, allowing blood to enter the glomerular capillaries more easily. The relatively greater resistance of the efferent arterioles causes blood to back up into the glomerular capillaries. The differences in the diameters raise the blood pressure in the glomerular capillaries, thus favoring filtration. In contrast, the colloid osmotic pressure of plasma in the glomerulus and the hydrostatic pressure inside the glomerular capsule oppose this movement. An increase in either of these pressures reduces filtration.

The sum of these forces is the **net filtration pressure**. Normally, net filtration pressure is always positive, causing filtration at the glomerulus (fig. 17.11).

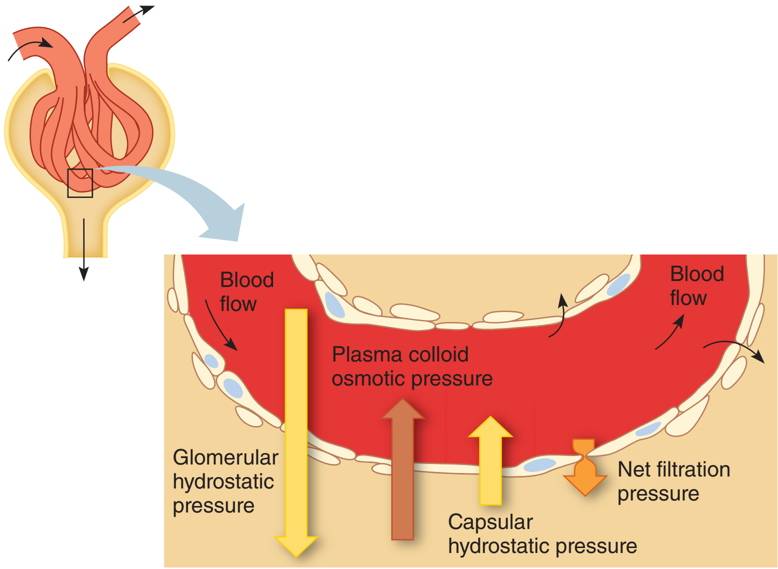
If arterial blood pressure plummets, as can occur during *shock*, glomerular hydrostatic pressure may fall below the level required for filtration. At the same time, epithelial cells of the renal tubules may not receive sufficient nutrients to maintain their high metabolic rates. As a result, tubular cells may die (tubular necrosis), impairing renal functions. Such changes can cause renal failure.

## Filtration Rate

The glomerular filtration rate (GFR), the most commonly measured index of kidney function, is directly proportional to net filtration pressure. Consequently, factors that affect glomerular hydrostatic pressure, glomerular plasma osmotic pressure, or hydrostatic pressure in the glomerular capsule also affect filtration rate. For example, any change in the diameters of the afferent and efferent arterioles changes glomerular hydrostatic pressure, also altering the glomerular filtration rate.

If the afferent arteriole, through which blood enters the glomerulus, constricts, filtration pressure will decrease. In contrast, if the efferent arteriole (through which blood leaves the glomerulus) constricts, blood backs up into the glomerulus and filtration pressure rises. Vasodilation of these vessels produces opposite effects. Stimulation by the sympathetic nervous system constricts both of these vessels, but the offsetting effects on filtration pressure keep GFR relatively constant.

In capillaries, the plasma colloid osmotic pressure that attracts water inward (see chapter 13, p. 367) opposes the blood pressure that forces water and dissolved substances outward. During glomerular filtration, proteins remaining in the plasma raise colloid osmotic pressure within the glomerular capillary. As the colloid osmotic pressure rises, net filtration pressure decreases but it is normally still sufficient to maintain filtration.


Blood flow
Blood flow
Plasma colloid osmotic pressure
Glomerular hydrostatic pressure
Net filtration pressure
Capsular hydrostatic pressure

| Net Outward Pressure | | |
|---|---|---|
| Outward force, glomerular hydrostatic pressure | = | +60 mm |
| Inward force of plasma colloid osmotic pressure | = | −32 mm |
| Inward force of capsular hydrostatic pressure | = | −18 mm |
| Net filtration pressure | = | +10 mm |

**FIGURE 17.11** Normally the glomerular net filtration pressure is positive, causing filtration. The forces involved include the hydrostatic and osmotic pressure of the plasma and the hydrostatic pressure of the fluid in the glomerular capsule.

Conditions that decrease plasma colloid osmotic pressure, such as a decrease in plasma protein concentration, increase the filtration rate.

In *glomerulonephritis,* the glomerular capillaries are inflamed and become more permeable to proteins, which appear in the glomerular filtrate and in urine (proteinuria). At the same time, the protein concentration in blood plasma decreases (hypoproteinemia), and this decreases plasma colloid osmotic pressure. As a result, less tissue fluid moves into the capillaries throughout the body, and edema develops.

The hydrostatic pressure in the glomerular capsule may rise because of an obstruction, such as a stone in a ureter or an enlarged prostate gland pressing on the urethra. Such a blockage causes fluid to back up into renal tubules and raise the hydrostatic pressure in the glomerular capsule. Any increase in capsular pressure opposes glomerular filtration, and the filtration rate may decrease significantly.

At rest, the kidneys receive about 25% of the cardiac output, and about 20% of the blood plasma is filtered as it flows through the glomerular capillary. This means that in an average adult, the GFR for the nephrons of both kidneys is about 125 milliliters per minute, or approximately 180 liters (nearly 45 gallons) in 24 hours. Of course, only a small fraction is excreted as urine. Instead, most of the fluid that passes through the renal tubules is reabsorbed and reenters the plasma.

**PRACTICE**

9. Which processes form urine?
10. Which forces affect net filtration pressure?
11. Which factors influence the rate of glomerular filtration?

## Regulation of Filtration Rate

The glomerular filtration rate is usually relatively constant. To help maintain homeostasis, however, the glomerular filtration rate may increase when body fluids are in excess and decrease when the body must conserve fluid.

Sympathetic nervous system reflexes that respond to changes in blood pressure and blood volume can cause vasoconstriction of both the afferent and the efferent arterioles. Afferent arteriole constriction helps maintain peripheral resistance and systemic blood pressure, but would lower filtration pressure. Simultaneous contraction of the efferent arteriole counteracts this effect on filtration pressure. Thus, systemic pressure is protected, but so is GFR. Conversely, vasodilation of afferent arterioles increases the glomerular filtration rate to counter increased blood volume or blood pressure.

Another mechanism to control filtration rate involves the enzyme *renin.* Juxtaglomerular cells secrete renin in response to three types of stimuli: (1) when special cells in the afferent arteriole sense a drop in blood pressure; (2) in response to sympathetic stimulation; and (3) when the macula densa (see fig. 17.8) senses decreased numbers of chloride, potassium, and sodium ions reaching the end of the ascending limb of the nephron loop. Once in the bloodstream, renin reacts with the plasma protein *angiotensinogen* to form *angiotensin I.* A second enzyme (*angiotensin-converting enzyme,* or ACE) in the lungs and in plasma quickly converts angiotensin I to *angiotensin II.*

Angiotensin II carries out a number of actions that help maintain sodium balance, water balance, and blood pressure (fig. 17.12). Angiotensin II vasoconstricts the efferent arteriole, which causes blood to back up into the glomerulus, raising filtration pressure. This important action helps minimize the decrease in glomerular filtration rate when systemic blood pressure is low. Angiotensin II has a major effect on the kidneys by stimulating secretion of the adrenal hormone aldosterone, which stimulates tubular reabsorption of sodium.

The heart secretes another hormone, *atrial natriuretic peptide* (ANP), when blood volume increases. ANP increases sodium excretion by a number of mechanisms, including increasing the glomerular filtration rate.

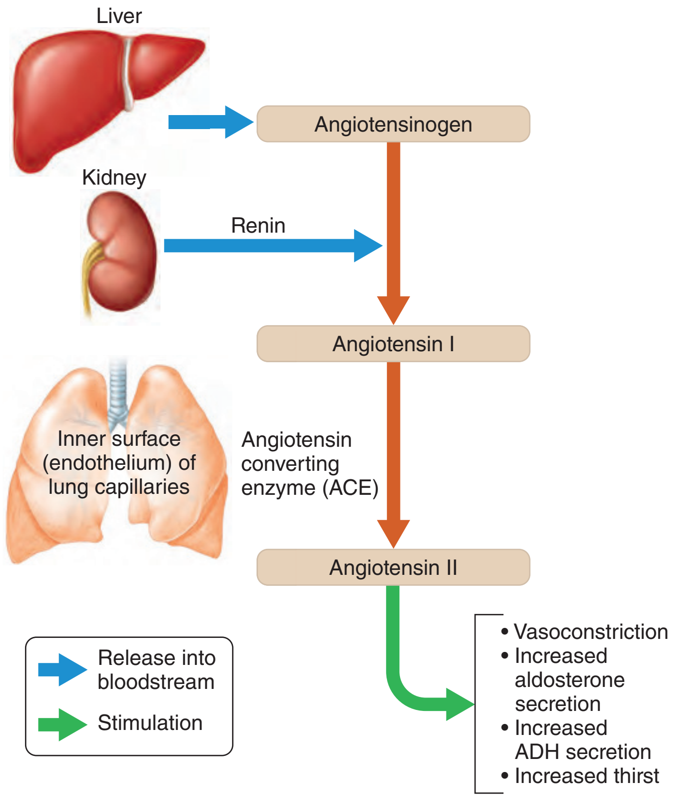

Liver
Angiotensinogen
Kidney
Renin
Angiotensin I
Inner surface (endothelium) of lung capillaries
Angiotensin converting enzyme (ACE)
Angiotensin II
• Vasoconstriction
• Increased aldosterone secretion
• Increased ADH secretion
• Increased thirst
Release into bloodstream
Stimulation

**FIGURE 17.12** The formation of angiotensin II in the bloodstream involves several organs and results in multiple actions that conserve sodium and water.

Elevated blood pressure (hypertension) is sometimes associated with excessive release of renin, followed by increased formation of the vasoconstrictor angiotensin II. Some patients with this form of high blood pressure may take a drug called an *angiotensin-converting enzyme inhibitor.* These "ACE inhibitors" prevent the formation of angiotensin II by inhibiting the action of the enzyme that converts angiotensin I into angiotensin II.

**PRACTICE**

12. What is the function of the macula densa?
13. How does renin help regulate filtration rate?

## Tubular Reabsorption

Comparing the composition of glomerular filtrate entering the renal tubule with that of urine leaving the tubule reveals that the fluid changes as it passes through the tubule (see table 17.1). For example, glucose is present in glomerular filtrate but absent in urine. In contrast, urea and uric acid are much more concentrated in urine than in glomerular filtrate. Such changes in fluid composition are largely the result of tubular reabsorption, the process that returns filtered substances to the bloodstream. In this process, substances are transported out of the tubular fluid, through the epithelium of the renal tubule, and into the interstitial fluid. These substances then diffuse into the peritubular capillaries (fig. 17.13).

Tubular reabsorption returns substances to the internal environment. The term *tubular* is used because the epithelial cells that make up the renal tubules carry out this process. In tubular reabsorption, substances must first cross the cell membrane facing the inside of the tubule and then cross the cell membrane facing the interstitial fluid.

The basic rules for movements across cell membranes apply to tubular reabsorption. Substances moving down a concentration gradient must be lipid-soluble, or there must be a carrier molecule or channel for that substance in the renal tubular cells. Active transport, requiring ATP, may move substances uphill against a concentration gradient.

Peritubular capillary blood is under relatively low pressure because it has already passed through two arterioles. Also, the walls of the peritubular capillaries are more permeable than other capillaries. Finally, because fluid is lost through glomerular filtration, the plasma protein concentration in the peritubular capillaries is relatively high. All of these factors enhance the rate of fluid reabsorption from the renal tubule.

Tubular reabsorption occurs throughout the renal tubule, but most of it takes place in the proximal convoluted portion. The epithelial cells here have many microscopic projections called *microvilli* that form a "brush border" on their free surfaces. These tiny extensions greatly increase the surface area exposed to glomerular filtrate and enhance reabsorption.

Segments of the renal tubule are adapted to reabsorb specific substances, using particular modes of transport. Active transport, for example, reabsorbs glucose through the walls of the proximal convoluted tubule. Water is then reabsorbed by osmosis through the epithelium of the proximal convoluted tubule. However, parts of the distal convoluted tubule and collecting duct may be almost impermeable to water. This is a characteristic important in regulating urine concentration and volume, described on page 493.

Active transport utilizes specific carrier molecules in cell membranes (see chapter 3, p. 76). These carriers transport certain molecules across the membrane, release them, and then repeat the process. However, such a mechanism has a *limited transport capacity;* that is, it can transport only a certain number of molecules in a given time because the number of carriers is limited.

Usually, glucose carrier molecules are able to transport all of the glucose in glomerular filtrate. But when the plasma glucose concentration increases to a critical level, called the *renal plasma threshold,* more glucose

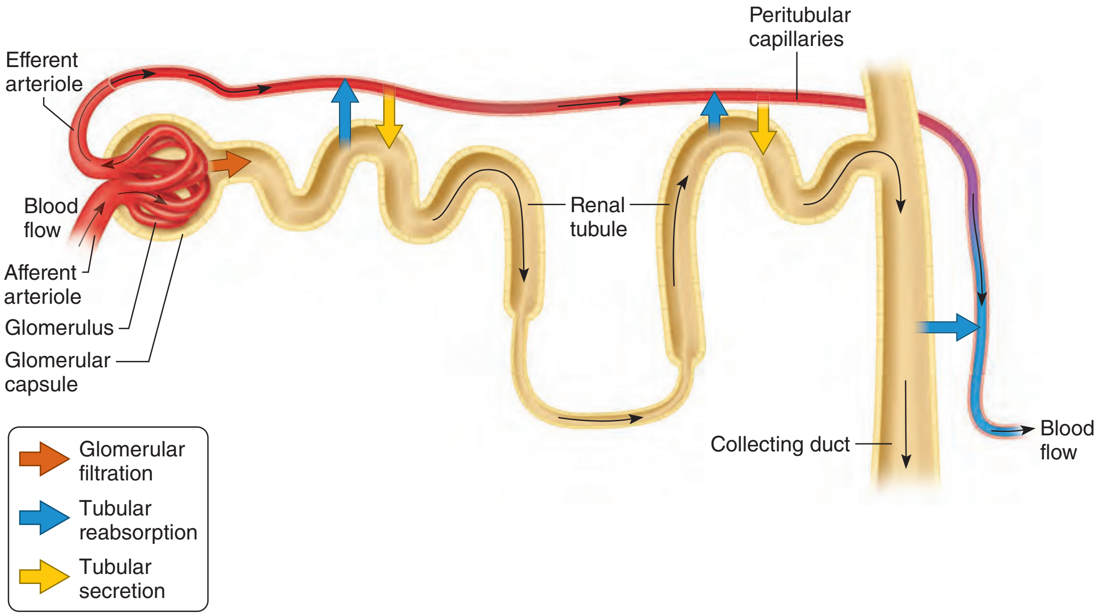


**FIGURE 17.13** Two processes in addition to glomerular filtration contribute to forming urine. (**a**) Tubular reabsorption transports substances from the tubular fluid into the blood within the peritubular capillary. (**b**) Tubular secretion transports substances from the blood within the peritubular capillary into the renal tubule.

**Q** *Which of the three processes (glomerular filtration, tubular reabsorption, tubular secretion), if increased for a substance, would reduce urinary excretion of that substance?*

**Answer can be found in Appendix F on page 582.**

molecules are in the filtrate than can be actively transported. As a result, some glucose remains in the tubular fluid and is excreted in urine.

Amino acids enter the glomerular filtrate and are reabsorbed in the proximal convoluted tubule. Three active transport mechanisms reabsorb different groups of amino acids whose members have similar structures. Normally, only a trace of amino acids remains in the urine.

Glomerular filtrate is nearly free of protein except for traces of albumin, a small protein that is taken up by endocytosis through the brush border of epithelial cells lining the proximal convoluted tubule. Once these proteins are inside an epithelial cell, they are broken down to amino acids, which then move into the blood of the peritubular capillary.

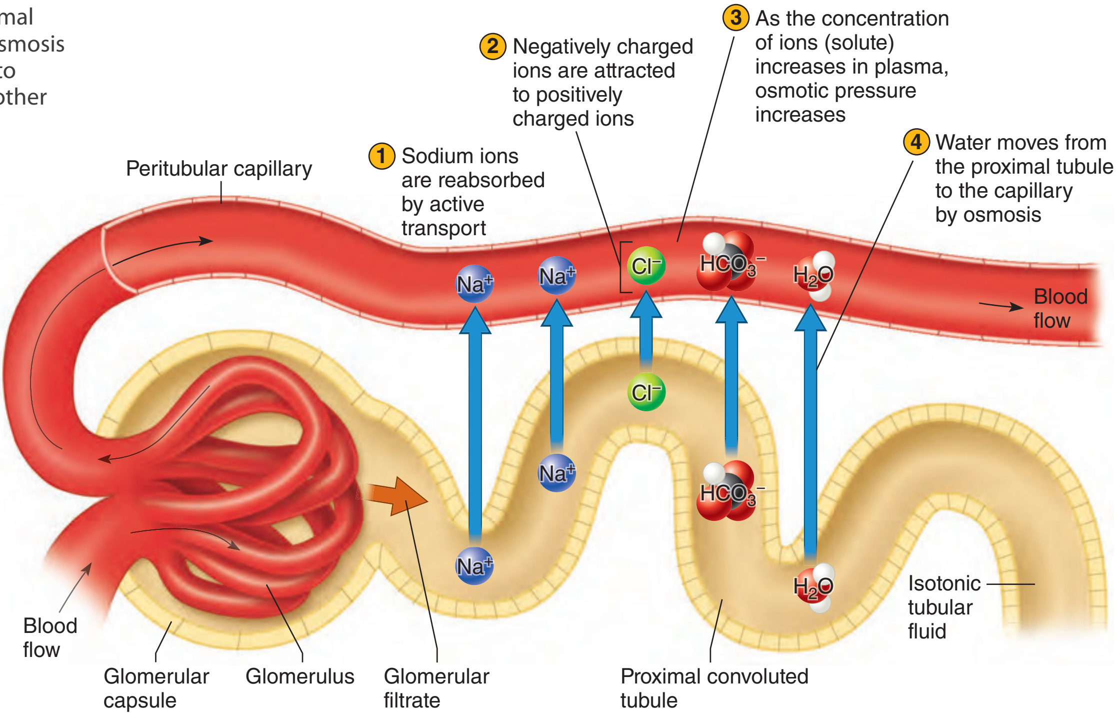
The epithelium of the proximal convoluted tubule reabsorbs other substances, including creatine; lactic, citric, uric, and ascorbic (vitamin C) acids; and phosphate, sulfate, calcium, potassium, and sodium ions. Active transport mechanisms with limited transport capacities reabsorb these chemicals. However, these substances usually do not appear in urine until glomerular filtrate concentration exceeds a particular substance's threshold.

## Sodium and Water Reabsorption

Substances that remain in the renal tubule become more concentrated as water is reabsorbed from the filtrate. Water reabsorption occurs passively by osmosis, primarily in the proximal convoluted tubule, and is closely associated with the active reabsorption of sodium ions. It increases if sodium reabsorption increases, and decreases if sodium reabsorption decreases.

Active transport (the sodium pump) reabsorbs about 70% of sodium ions in the proximal segment of the renal tubule. As these positively charged ions ($Na^+$) move through the tubular wall, negatively charged ions, including chloride ions ($Cl^-$) and bicarbonate ions ($HCO_3^-$), accompany them. These negatively charged ions move because of the electrochemical attraction between particles of opposite charge. This is a form of *passive transport* because it does not require direct expenditure of cellular energy (fig. 17.14).

As active transport moves more sodium ions out of the proximal tubule, along with (passively) various negatively charged ions, the concentration of solutes within the peritubular blood increases. Because water moves across cell membranes from regions of lesser solute concentration toward regions of greater solute concentration, water moves by osmosis from the renal tubule into the peritubular capillary. Movement of solutes and water into the peritubular capillary greatly reduces the



① Sodium ions are reabsorbed by active transport
② Negatively charged ions are attracted to positively charged ions
③ As the concentration of ions (solute) increases in plasma, osmotic pressure increases
④ Water moves from the proximal tubule to the capillary by osmosis
Peritubular capillary
$Na^+$
$Na^+$
$Cl^-$
$HCO_3^-$
$H_2O$
Blood flow
$Cl^-$
$Na^+$
$HCO_3^-$
$Na^+$
$H_2O$
Isotonic tubular fluid
Blood flow
Glomerular capsule
Glomerulus
Glomerular filtrate
Proximal convoluted tubule

**FIGURE 17.14** In the proximal portion of the renal tubule, osmosis reabsorbs water in response to reabsorption of sodium and other solutes.

fluid volume within the renal tubule. The end of the proximal convoluted tubule is in osmotic equilibrium, and the remaining tubular fluid is isotonic (fig. 17.14).

Active transport continues to reabsorb sodium ions as the tubular fluid moves through the nephron loop, the distal convoluted tubule, and the collecting duct. Water is absorbed passively by osmosis in various segments of the renal tubule. As a result, almost all the sodium ions and water that enter the renal tubule as part of the glomerular filtrate are reabsorbed before urine is excreted.

## PRACTICE

14. Which chemicals are normally present in the glomerular filtrate but not in urine?
15. Which mechanisms reabsorb solutes from the glomerular filtrate?
16. Describe the role of passive transport in urine formation.

## Tubular Secretion

About 20% of the plasma flowing through the kidneys is filtered in the glomeruli, and approximately 80% escapes filtration and continues on through the peritubular capillaries. In tubular secretion, certain substances move from the plasma of blood in the peritubular capillary into the fluid of the renal tubule. As a result, the amount of a particular chemical excreted in the urine may exceed the amount filtered from the plasma in the glomerulus (see fig. 17.13). The term *tubular* is used because the epithelial cells of the renal tubules carry out the process, as they do in tubular reabsorption.

Active transport mechanisms similar to those that function in reabsorption secrete some substances. Secretory mechanisms, however, transport substances in the opposite direction. For example, the epithelium of the proximal convoluted segment actively secretes certain organic compounds, including creatinine, histamine, and the drug penicillin, into the tubular fluid.

Hydrogen ions are also actively secreted throughout the entire renal tubule. Secretion of hydrogen ions is important in regulating the pH of body fluids, as chapter 18 (p. 512) explains.

Most potassium ions in the glomerular filtrate are actively reabsorbed in the proximal convoluted tubule, but some may be secreted in the distal segment and collecting duct. During this process, active reabsorption of sodium ions from the tubular fluid results in a negative electrical charge within the tubule. Because positively charged potassium ions ($K^+$) and hydrogen ions ($H^+$) are attracted to negatively charged regions, these ions move passively through the tubular epithelium and enter the tubular fluid (fig. 17.15). Potassium ions are also secreted by active processes.

To summarize, urine forms as a result of the following:

- Glomerular filtration of materials from blood plasma.
- Reabsorption of substances, including glucose; water; creatine; amino acids; lactic, citric, and uric acids; and phosphate, sulfate, calcium, potassium, and sodium ions.
- Secretion of substances, including penicillin, histamine, phenobarbital, hydrogen ions, ammonia, and potassium ions.

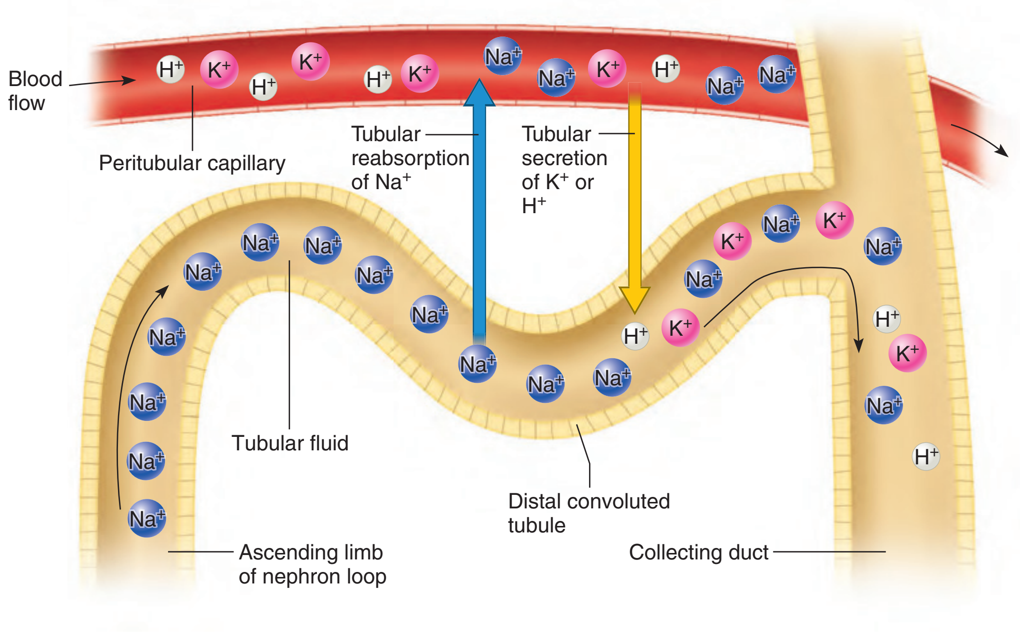

Blood flow
Peritubular capillary
Tubular reabsorption of $Na^+$
Tubular secretion of $K^+$ or $H^+$
Tubular fluid
Distal convoluted tubule
Collecting duct
Ascending limb of nephron loop

**FIGURE 17.15** In the distal convoluted tubule, potassium ions (and hydrogen ions) may be passively secreted in response to the active reabsorption of sodium ions.

**PRACTICE**

17. Define *tubular secretion.*
18. Which substances are actively secreted?
19. How does sodium reabsorption affect potassium secretion?

## Regulation of Urine Concentration and Volume

The hormones aldosterone and ADH (antidiuretic hormone) may stimulate additional reabsorption of sodium and water, respectively. The changes in sodium and water excretion in response to these hormones are the final adjustments the kidney makes to maintain a constant internal environment.

The adrenal glands secrete aldosterone in response to changes in the blood concentrations of sodium and potassium ions (see chapter 11, p. 315). Aldosterone stimulates the distal convoluted tubule to reabsorb sodium and secrete potassium. Angiotensin II is another important stimulator of aldosterone secretion.

Neurons in the hypothalamus produce ADH, which the posterior pituitary releases in response to a decreasing water concentration in blood or a decrease in blood volume. When ADH reaches the kidney, it increases the water permeability of the epithelial linings of the distal convoluted tubule and collecting duct, and water moves rapidly out of these segments by osmosis—that is, water is reabsorbed. Urine volume falls, and soluble wastes and other substances become more concentrated, which minimizes loss of body fluids when dehydration is likely.

If body fluids have excess water, ADH secretion decreases. As blood levels of ADH drop, the epithelial linings of the distal segment and collecting duct become less permeable to water, less water is reabsorbed, and urine is more dilute, excreting the excess water. Table 17.2 summarizes the role of ADH in urine production.

## Urea and Uric Acid Excretion

**Urea** (u-re′ah) is a by-product of amino acid catabolism. Consequently, its plasma concentration reflects the amount of protein in the diet. Urea enters the renal tubule by filtration. About 80% of it is reabsorbed, and the remainder is excreted in urine.

**Uric acid** is a product of the metabolism of certain organic bases in nucleic acids. Active transport reabsorbs all the uric acid normally present in glomerular filtrate, but a small amount is secreted into the renal tubule and is excreted in urine. Table 17.3 summarizes some specific functions of the nephron segments and the collecting duct.

Excess uric acid may precipitate in the plasma and be deposited as crystals in joints, causing the inflammation and extreme pain of gout, particularly in the digits and especially in the great toe. Gout has had an interesting history. Hippocrates mentioned it. King Charles I of Spain gave up his vast empire in 1556 due to the painful condition. In 2006, Spanish researchers confirmed the diagnosis by detecting uric acid deposits in the terminal joint of a finger that, for reasons unknown, had been preserved in a small box apart from the rest of the king's body. Today, gout is treated with drugs that inhibit uric acid reabsorption or block an enzyme in the biosynthetic pathway for uric acid. Limiting foods rich in uric acid, such as organ meats and seafood, and drinking more water to dilute the urine can help. Gout is inherited, but an attack may not occur until the person eats the offending foods.

**TABLE 17.2 Role of ADH in Regulating Urine Concentration and Volume**

1. Concentration of water in blood decreases.
2. Increase in osmotic pressure of body fluids stimulates osmoreceptors in hypothalamus of brain.
3. Hypothalamus signals posterior pituitary to release ADH.
4. Blood carries ADH to kidneys.
5. ADH causes distal convoluted tubules and collecting ducts to increase water reabsorption by osmosis.
6. Urine becomes concentrated, and urine volume decreases.

**PRACTICE**

20. How does the hypothalamus regulate urine concentration and volume?
21. Explain how urea and uric acid are excreted.

## Urine Composition

Urine composition reflects the volumes of water and amounts of solutes that the kidneys must eliminate from the body or retain in the internal environment to maintain homeostasis. The kidney is able to accomplish this because it handles each of the substances discussed above independently. Urinary excretion of some solutes may increase while that of other solutes may decrease. Urine composition varies considerably from time to time because of variations in dietary intake and physical activity. About 95% water, urine usually contains urea and uric acid. It may also have a trace of amino acids and a variety of electrolytes, whose concentrations vary directly with amounts in the diet (see table 17.1).

The volume of urine produced is usually between 0.6 and 2.5 liters per day, depending on fluid intake, environmental temperature and relative humidity of the surrounding air, as well as the person's emotional condition, respiratory rate, and body temperature. Urine output of 50–60 milliliters per hour is normal; output of less than 30 milliliters per hour may indicate kidney failure.

Glucose, proteins, ketones, and blood cells are not usually found in urine. These unusual urinary components may reflect certain normal circumstances, or disease. For example, glucose in urine may follow a large intake of carbohydrates, precede giving birth, or be due to diabetes mellitus (see Clinical Application 11.1, pp. 318–319). Proteins may appear following vigorous physical exercise, and ketones may appear after a prolonged fast.

**TABLE 17.3 Functions of Nephron Components**

| Part | Function |
|---|---|
| Renal corpuscle | |
| Glomerulus | Filtration of water and dissolved substances from plasma |
| Glomerular capsule | Receives glomerular filtrate |
| Renal tubule | |
| Proximal convoluted tubule | Reabsorption of glucose; amino acids; creatine; lactic, uric, citric, and ascorbic acids; phosphate, sulfate, calcium, potassium, and sodium ions by active transport<br>Reabsorption of water by osmosis<br>Reabsorption of chloride ions and other negatively charged ions by electrochemical attraction<br>Active secretion of substances such as penicillin, histamine, creatinine, and hydrogen ions |
| Descending limb of nephron loop | Reabsorption of water by osmosis |
| Ascending limb of nephron loop | Reabsorption of sodium, potassium, and chloride ions by active transport |
| Distal convoluted tubule | Reabsorption of sodium ions by active transport<br>Reabsorption of water by osmosis<br>Secretion of hydrogen and potassium ions both actively and passively by electrochemical attraction |
| Collecting duct | Reabsorption of water by osmosis (Although the collecting duct is not anatomically part of the nephron, it is included here because of its functional importance in urine formation.) |

**PRACTICE**

22. List the normal constituents of urine.
23. Which factors affect urine volume?

## 17.4 | Urine Elimination

After urine forms in the nephrons, it passes from the collecting ducts through openings in the renal papillae and enters the calyces of the kidney (see fig. 17.2). From there, it passes through the renal pelvis, and a ureter conveys it to the urinary bladder (see fig. 17.1, 17.7, and reference plate 6, p. 37). The urethra passes urine to the outside.

### Ureters

Each **ureter** (u-re′ter) is a tube about 25 centimeters long that begins as the funnel-shaped renal pelvis. It descends behind the parietal peritoneum and runs parallel to the vertebral column. In the pelvic cavity, each ureter courses forward and medially, joining the urinary bladder from underneath.

The ureter wall has three layers. The inner layer, or *mucous coat,* is continuous with the linings of the renal tubules and the urinary bladder. The middle layer, or *muscular coat,* consists largely of smooth muscle fibers. The outer layer, or *fibrous coat,* is connective tissue (fig. 17.16).

Movements of the muscular walls of the ureters propel the urine. Muscular peristaltic waves, originating in the renal pelvis, force urine along the length of the ureter. When a peristaltic wave reaches the urinary bladder, a jet of urine spurts through a fold of mucous membrane that surrounds the opening, and the urine enters. Because of the angle at which the ureters enter the bladder, the bladder wall acts as a valve, allowing urine to enter the bladder from the ureter but preventing it from flowing backwards as the bladder fills. Clinical Application 17.1 discusses kidney stones, which cause sharp pain when they enter a ureter.

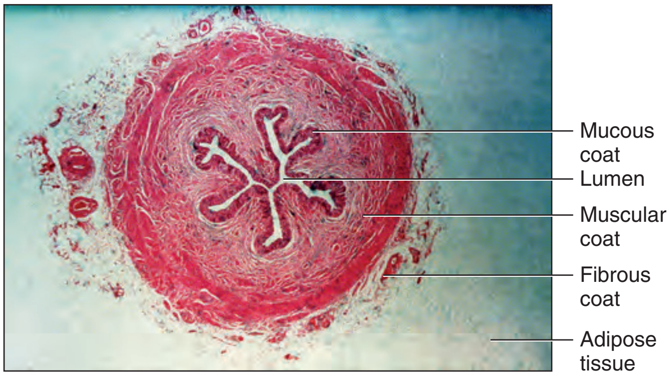


**FIGURE 17.16** APR Cross section of a ureter (75×).

**PRACTICE**

24. Describe the structure of a ureter.
25. How is urine moved from the renal pelvis to the urinary bladder?
26. What prevents urine from backing up from the urinary bladder into the ureters?

### Urinary Bladder

The **urinary bladder** is a hollow, distensible, muscular organ that stores urine and forces it into the urethra (see fig. 17.1 and reference plate 6, p. 37). The bladder is in the pelvic cavity, behind the pubic symphysis and beneath the parietal peritoneum.

The pressure of surrounding organs alters the bladder's somewhat spherical shape. When empty, the inner wall of the bladder forms many folds, but as the bladder fills with urine, the wall becomes smoother. At the same time, the superior surface of the bladder expands upward into a dome.

The internal floor of the bladder includes a triangular area called the *trigone,* which has an opening at each of its three angles (fig. 17.17*a*). Posteriorly, at the base of the trigone, the openings are those of the ureters. Anteriorly, at the apex of the trigone, a short, funnel-shaped extension called the *neck* of the bladder contains the opening into the urethra.

The wall of the urinary bladder has four layers. The inner layer, or *mucous coat,* includes several layers of transitional epithelial cells. The thickness of this tissue changes as the bladder expands and contracts. During distension, the tissue may be only two or three cells thick; during contraction, it may be five or six cells thick (see fig. 5.9, p. 112).

The second layer of the bladder wall is the *submucous coat.* It consists of connective tissue and has many elastic fibers. The third layer of the bladder wall, or *muscular coat,* is composed primarily of coarse bundles of smooth muscle fibers. These bundles are interlaced in all directions and at all depths, and together they comprise the **detrusor muscle** (de-truz′or mus′l). The part of the detrusor muscle that surrounds the neck of the bladder forms an *internal urethral sphincter.* Sustained contraction of this muscle prevents the bladder from emptying until pressure in the bladder increases to a certain level. The detrusor muscle is innervated with parasympathetic nerve fibers that function in the micturition reflex, discussed in the next section.

## CLINICAL APPLICATION 17.1

### Kidney Stones

Kidney stones, which are usually composed of uric acid, calcium oxalate, calcium phosphate, or magnesium phosphate, can form in the collecting ducts and renal pelvis (fig. 17A). Such a stone passing into a ureter causes sudden, severe pain that begins in the region of the kidney and radiates into the abdomen, pelvis, and lower limbs. It may also cause nausea and vomiting, and blood in the urine.

About 60% of kidney stones pass from the body on their own. Other stones were once removed surgically but are now shattered with intense sound waves. In this procedure, called *extracorporeal shock-wave lithotripsy (ESWL)*, the patient is placed in a stainless steel tub filled with water. A spark-gap electrode produces underwater shock waves, and a reflector concentrates and focuses the shock-wave energy on the stones. The resulting sandlike fragments then leave in urine.

The tendency to form kidney stones is inherited, particularly the stones that contain calcium, which account for more than half of all cases. Eating calcium-rich foods does not increase the risk, but taking calcium supplements can. People who have calcium oxalate stones can reduce the risk of recurrence by avoiding specific foods: chocolate, coffee, wheat bran, cola, strawberries, spinach, nuts, and tea. Other causes of kidney stones include excess vitamin D, blockage of the urinary tract, or a complication of a urinary tract infection.

It is very helpful for a physician to analyze the composition of the stones, because certain drugs can prevent recurrence. Stones can be collected during surgery or by the person, using a special collection device.

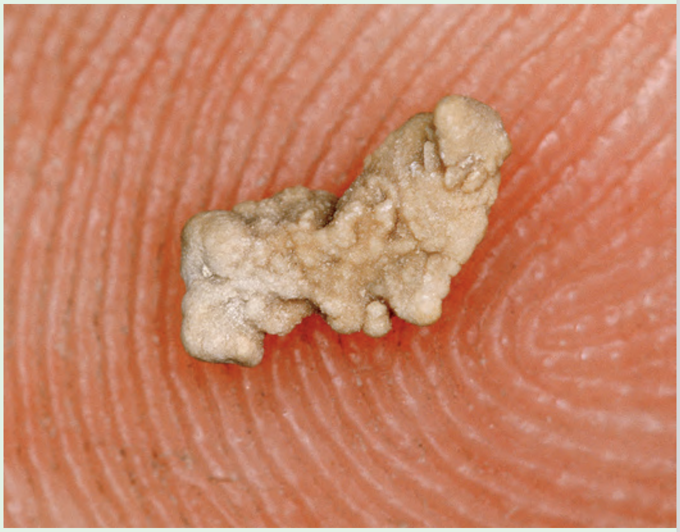


**FIGURE 17A** This kidney stone is small, held against this fingertip, but it is large enough to cause severe pain.

The outer layer of the bladder wall, or *serous coat*, consists of the parietal peritoneum. This layer is only on the bladder's upper surface. Elsewhere, the outer coat is connective tissue (fig. 17.17*b*).

Inflammation of the urinary bladder, called *cystitis*, is more common in women than in men because the female urethral pathway is shorter, making it easier for bacteria to enter from the outside. Infectious agents, such as bacteria, may ascend from the urinary bladder into the ureters because the linings of these structures are continuous. Inflammation of the ureter is called *ureteritis*.

### PRACTICE

27. Describe the trigone of the urinary bladder.
28. Describe the structure of the bladder wall.
29. What kind of nerve fibers supply the detrusor muscle?

## Micturition APR

**Micturition** (mik″tu-rish′un), or urination, is the process that expels urine from the urinary bladder. In micturition, the detrusor muscle contracts, as do muscles in the abdominal wall and pelvic floor. At the same time, muscles in the thoracic wall and diaphragm do not contract. Micturition also requires relaxation of the *external urethral sphincter*. This muscle, which is part of the urogenital diaphragm described in chapter 8 (pp. 212–214), surrounds the urethra about 3 centimeters from the urinary bladder and is composed of voluntary skeletal muscle tissue.

Distension of the bladder wall as it fills with urine stimulates stretch receptors, triggering the micturition reflex. The *micturition reflex center* is in the spinal cord. When sensory impulses from the stretch receptors signal the reflex center, parasympathetic motor impulses travel to the detrusor muscle, which contracts rhythmically in response. A sensation of urgency accompanies this action.

The urinary bladder may hold as much as 600 milliliters of urine before stimulating pain receptors, but the urge to urinate usually begins when it contains about

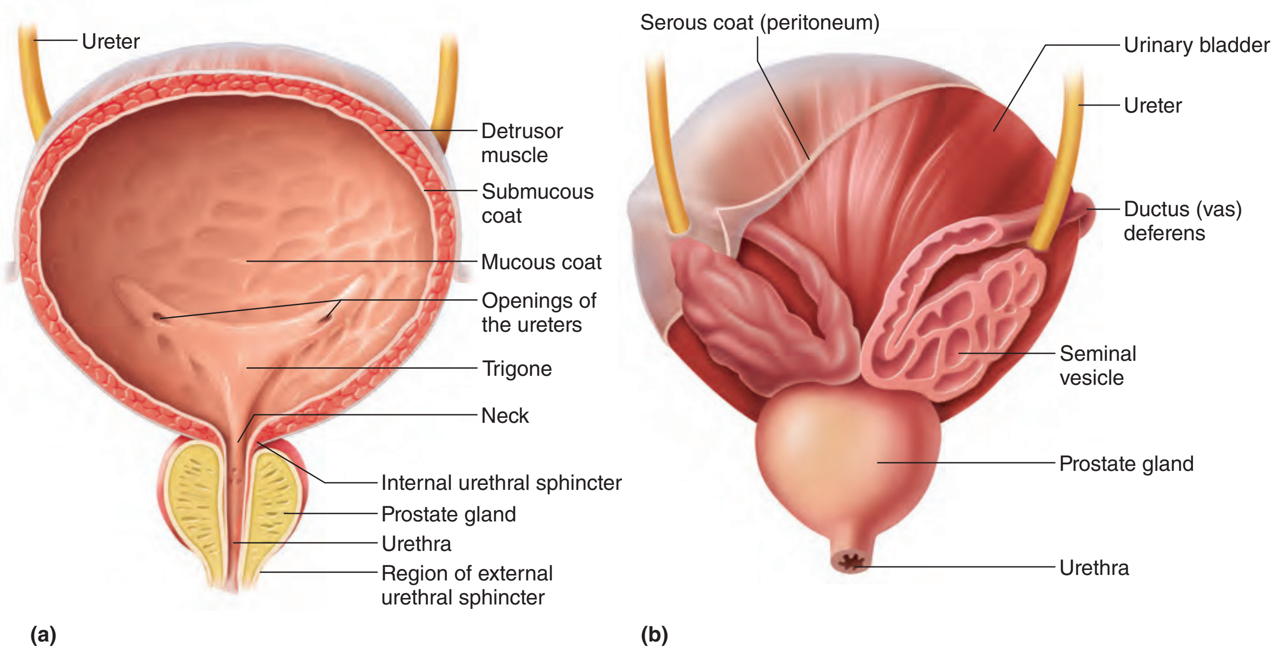

Ureter
Detrusor muscle
Submucous coat
Mucous coat
Openings of the ureters
Trigone
Neck
Internal urethral sphincter
Prostate gland
Urethra
Region of external urethral sphincter
(a)
Serous coat (peritoneum)
Urinary bladder
Ureter
Ductus (vas) deferens
Seminal vesicle
Prostate gland
Urethra
(b)

**FIGURE 17.17** APR A urinary bladder in a male. (**a**) Longitudinal section. (**b**) Posterior view.

150 milliliters. As urine volume increases to 300 milliliters or more, the sensation of fullness intensifies, and contractions of the bladder wall become more powerful. When these contractions are strong enough to force the internal urethral sphincter open, another reflex signals the external urethral sphincter to relax, and the bladder can empty.

The external urethral sphincter is composed of skeletal muscle. Therefore it is under conscious control, and typically it is contracted until a person decides to urinate. Nerve centers in the brainstem and cerebral cortex that can partially inhibit the micturition reflex aid this control. When a person decides to urinate, the external urethral sphincter relaxes and the micturition reflex is no longer inhibited. Nerve centers in the pons and the hypothalamus of the brain facilitate the micturition reflex. Then the detrusor muscle contracts, and urine is excreted through the urethra. Within a few moments, the neurons of the micturition reflex undergo adaptation, the detrusor muscle relaxes, and the urinary bladder begins to fill with urine again.

Damage to the spinal cord above the sacral region destroys the sensation of fullness and the voluntary control of urination. However, if the micturition reflex center and its sensory and motor fibers are uninjured, micturition may continue to occur reflexly. In this case, the urinary bladder collects urine until its walls stretch enough to trigger a micturition reflex, and the detrusor muscle contracts in response. This condition is called an *automatic bladder.*

## Urethra

The **urethra** (u-re′thrah) is a tube that conveys urine from the urinary bladder to the outside (see fig. 17.1 and reference plate 7, p. 38). Its wall is lined with mucous membrane and has a thick layer of smooth muscle tissue, whose fibers are generally directed longitudinally. The urethral wall also has abundant mucous glands, called *urethral glands,* which secrete mucus into the urethral canal (fig. 17.18).

In a female, the urethra is about 4 centimeters long. Its opening, the *external urethral orifice* (urinary meatus) is anterior to the vaginal opening and posterior to the clitoris. In a male, the urethra functions as part of both the urinary system and the reproductive system and extends from the urinary bladder to the tip of the penis.

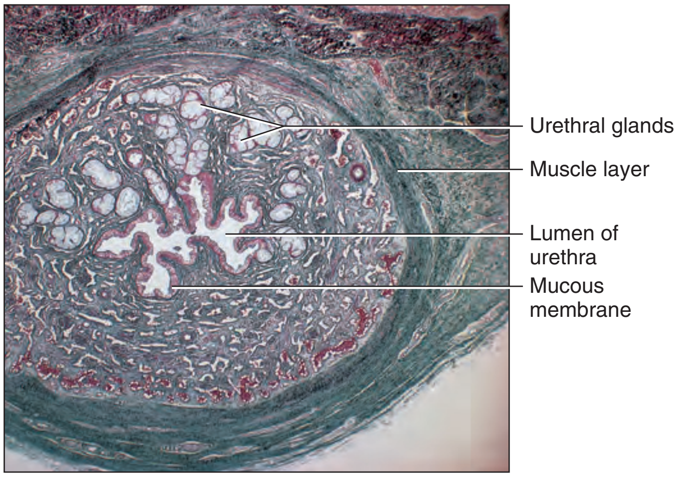

Urethral glands
Muscle layer
Lumen of urethra
Mucous membrane

**FIGURE 17.18** Cross section through the urethra (10×).

In a urinary tract infection (UTI), urination is frequent, painful, scant, and may be bloody, with accompanying pelvic pain. Usually pathogenic bacteria in the urinary tract remain outside the cells, and they are easily killed with antibiotic drugs or prevented from attaching to ureter lining cells by exposure to compounds in cranberry and blueberry juices that the person drinks. However, certain bacteria, such as *Escherichia coli,* can enter the lining cells of the bladder, persisting inside the cells and causing recurrent UTIs.

## PRACTICE

30. Describe micturition.
31. How is it possible to consciously inhibit the micturition reflex?
32. Describe the structure of the urethra.

## Summary Outline

### 17.1 Introduction (p. 480)

*The urinary system consists of the kidneys, ureters, urinary bladder, and urethra.*

### 17.2 Kidneys (p. 480)

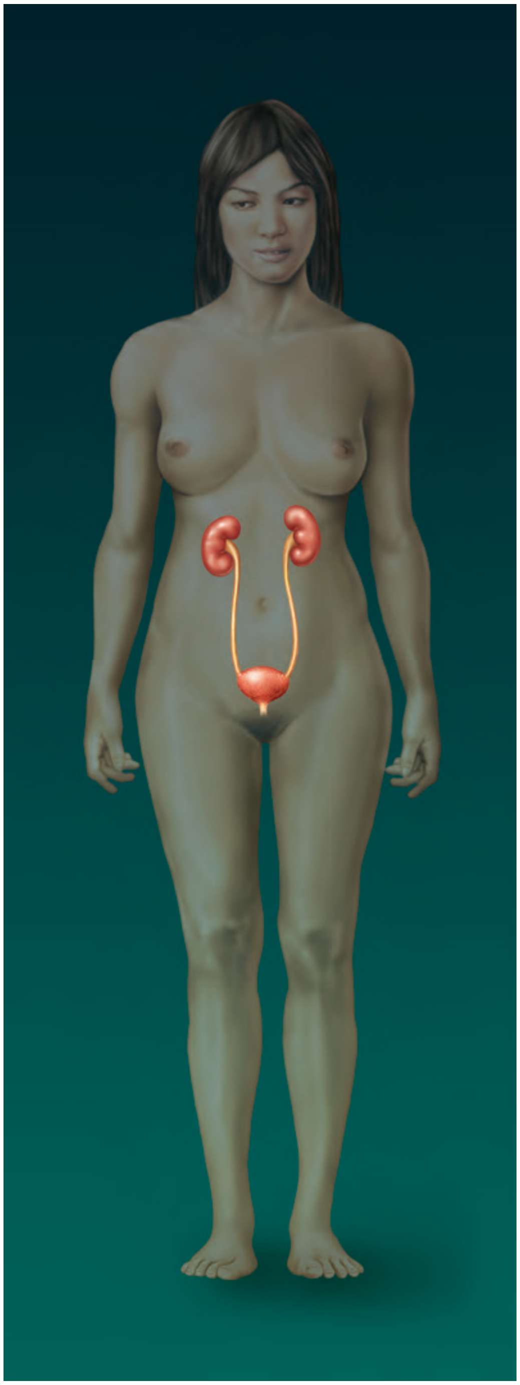
1. Location of the kidneys
    a. The kidneys are high on the posterior wall of the abdominal cavity.
    b. They are behind the parietal peritoneum.
2. Kidney structure
    a. A kidney has a hollow renal sinus.
    b. The ureter expands into the renal pelvis.
    c. Renal papillae project into the renal sinus.
    d. Each kidney is divided into a medulla and a cortex.
3. Kidney functions
    a. The kidneys maintain homeostasis by removing metabolic wastes from blood and excreting them.
    b. They also help regulate red blood cell production; blood volume and blood pressure; and the volume, composition, and pH of body fluids.
4. Renal blood vessels
    a. Arterial blood flows through the renal artery, interlobar arteries, arcuate arteries, cortical radiate arteries, and afferent arterioles to the nephrons.
    b. Venous blood returns through a series of vessels that correspond to the arterial pathways.
5. Nephrons
    a. Nephron structure
        (1) A nephron is the functional unit of the kidney.
        (2) It consists of a renal corpuscle and a renal tubule.
            (a) The corpuscle consists of a glomerulus and a glomerular capsule.
            (b) Segments of the renal tubule include the proximal convoluted tubule, nephron loop (descending and ascending limbs), and distal convoluted tubule, which empties into a collecting duct.
        (3) The collecting duct (technically not part of a nephron) empties into the minor calyx of the renal pelvis.
    b. Blood supply of a nephron
        (1) The glomerular capillary receives blood from the afferent arteriole and passes it to the efferent arteriole.
        (2) The efferent arteriole gives rise to the peritubular capillary system, which surrounds the renal tubule.
    c. Juxtaglomerular apparatus
        (1) The juxtaglomerular apparatus is at the point of contact between the last portion of the ascending limb of the nephron loop and the afferent and efferent arterioles.
        (2) It consists of the macula densa and juxtaglomerular cells.

### 17.3 Urine Formation (p. 485)

*Nephrons remove wastes from blood and regulate water and electrolyte concentrations. Urine is the end product.*

1. Glomerular filtration
    a. Urine formation begins when water and dissolved materials filter out of glomerular capillaries.
    b. Glomerular capillaries are much more permeable than the capillaries in other tissues.
    c. The composition of the filtrate is similar to that of tissue fluid.
2. Filtration pressure
    a. Filtration is due mainly to hydrostatic pressure inside glomerular capillaries.
    b. The osmotic pressure of plasma in the glomerular capillaries and the hydrostatic pressure in the glomerular capsule also affect filtration.
    c. Net filtration pressure is the net force moving material out of the glomerular capillaries and into the glomerular capsule.
3. Filtration rate
    a. Rate of filtration varies with filtration pressure.
    b. Filtration pressure changes with the diameters of the afferent and efferent arterioles.
    c. As colloid osmotic pressure in the glomerulus increases, filtration rate decreases.
    d. As hydrostatic pressure in a glomerular capsule increases, filtration rate decreases.
    e. The kidneys produce about 125 milliliters of glomerular fluid per minute, most of which is reabsorbed.
4. Regulation of filtration rate
    a. Glomerular filtration rate (GFR) remains relatively constant, but may increase or decrease as required.
    b. Increased activity of the sympathetic nervous system can maintain blood pressure with minimal change in GFR.
    c. When the macula densa senses decreased amounts of chloride, potassium, and sodium ions in the last part of the ascending limb of the nephron loop, it causes juxtaglomerular cells to release renin.
    d. This triggers a series of changes leading to vasoconstriction of afferent and efferent arterioles, which minimizes any decrease in glomerular filtration rate, and stimulates aldosterone secretion, which stimulates tubular sodium reabsorption.
5. Tubular reabsorption
    a. Substances are selectively reabsorbed from glomerular filtrate.
    b. The peritubular capillary's permeability adapts it for reabsorption.
    c. Most reabsorption occurs in the proximal tubule, where epithelial cells have microvilli.

# Urinary System

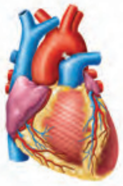


The urinary system controls the composition of the internal environment.

### Integumentary System

The urinary system compensates for water loss due to sweating. The kidneys and skin both play a role in vitamin D production.

### Cardiovascular System



The urinary system controls blood volume. Blood volume and blood pressure play a role in determining water and solute excretion.

### Skeletal System

The kidneys and bone tissue work together to control plasma calcium levels.

### Lymphatic System

The kidneys control extracellular fluid volume and composition (including lymph).

### Muscular System

Muscle tissue controls urine elimination from the bladder.

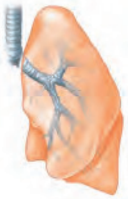
### Digestive System

The kidneys compensate for fluids lost by the digestive system.

### Nervous System

The nervous system influences urine production and elimination.

### Respiratory System



The kidneys and the lungs work together to control the pH of the internal environment.

### Endocrine System

The endocrine system influences urine production.

### Reproductive System

The urinary system in males shares organs with the reproductive system. The kidneys compensate for fluids lost from the male and female reproductive systems.

   d. Different modes of transport reabsorb various substances in particular segments of the renal tubule.
      (1) Active transport reabsorbs glucose and amino acids.
      (2) Osmosis reabsorbs water.
   e. Active transport mechanisms have limited transport capacities.
6. Sodium and water reabsorption
   a. Substances that remain in the filtrate are concentrated as water is reabsorbed.
   b. Active transport reabsorbs sodium ions.
   c. As positively charged sodium ions move out of the filtrate, negatively charged ions follow them.
   d. Water is passively reabsorbed by osmosis.
7. Tubular secretion
   a. Secretion transports substances from plasma in the peritubular capillaries to the renal tubular fluid.
   b. Various organic compounds are secreted actively.
   c. Potassium and hydrogen ions are secreted both actively and passively.
8. Regulation of urine concentration and volume
   a. Most sodium is reabsorbed before urine is excreted.
   b. Antidiuretic hormone increases the permeability of the distal convoluted tubule and collecting duct, promoting water reabsorption.
9. Urea and uric acid excretion
   a. Diffusion passively reabsorbs 80% of the urea.
   b. Active transport reabsorbs uric acid. Some uric acid is secreted into the renal tubule.
10. Urine composition
   a. Urine is about 95% water, and it also usually contains urea and uric acid.
   b. Urine contains varying amounts of electrolytes and may contain a trace of amino acids.
   c. Urine volume varies with fluid intake, certain environmental factors, and a person's emotional condition, respiratory rate, and body temperature.

**17.4 Urine Elimination (p. 495)**

1. Ureters
   a. The ureter extends from the kidney to the urinary bladder.
   b. Peristaltic waves in the ureter force urine to the urinary bladder.
2. Urinary bladder
   a. The urinary bladder stores urine and forces it through the urethra during micturition.
   b. The openings for the ureters and urethra are at the three angles of the trigone.
   c. A portion of the detrusor muscle forms an internal urethral sphincter.
3. Micturition
   a. Micturition expels urine.
   b. Micturition contracts the detrusor muscle and relaxes the external urethral sphincter.
   c. Micturition reflex
      (1) Distension stimulates stretch receptors in the bladder wall.
      (2) The micturition reflex center in the spinal cord sends parasympathetic motor impulses to the detrusor muscle.
      (3) As the bladder fills, its internal pressure increases, forcing the internal urethral sphincter open.
      (4) A second reflex relaxes the external urethral sphincter unless voluntary control maintains its contraction.
      (5) Nerve centers in the cerebral cortex and brainstem aid control of urination.
4. Urethra
   The urethra conveys urine from the urinary bladder to the outside.

## CHAPTER ASSESSMENTS

### 17.1 Introduction

**1.** Name and identify the general functions of the organs of the urinary system. (p. 480)

### 17.2 Kidneys

**2.** Explain why the kidneys are said to be retroperitoneal. (p. 481)
**3.** Describe the external and internal structure of a kidney. (p. 481)
**4.** Identify the functions of the kidneys. (p. 482)
**5.** List in correct order the vessels through which blood passes as it travels from the renal artery to the renal vein. (pp. 482–483 and 485)
**6.** Distinguish between a renal corpuscle and a renal tubule. (p. 483)
**7.** Name in correct order the parts of the nephron through which fluid passes from the glomerulus to the collecting duct. (p. 483)
**8.** Describe the location and structure of the juxtaglomerular apparatus. (p. 485)

### 17.3 Urine Formation

**9.** Which one of the following is abundant in blood plasma, but only in small amounts in glomerular filtrate? (p. 487)
a. sodium ions
b. water
c. glucose
d. protein

**10.** Define *net filtration pressure.* (p. 488)
**11.** Explain how the diameters of the afferent and efferent arterioles affect the rate of glomerular filtration. (p. 488)
**12.** Explain how changes in the osmotic pressure of blood plasma affect the glomerular filtration rate. (p. 488)
**13.** Explain how the hydrostatic pressure of a glomerular capsule affects the rate of glomerular filtration. (p. 489)
**14.** Describe two mechanisms by which the body regulates filtration rate. (p. 489)
**15.** Discuss how tubular reabsorption is selective. (p. 490)
**16.** Explain how the peritubular capillary is adapted for reabsorption. (p. 490)
**17.** Explain how epithelial cells of the proximal convoluted tubule are adapted for reabsorption. (p. 490)
**18.** Explain why active transport mechanisms have limited transport capacities. (p. 490)
**19.** Define *renal plasma threshold.* (pp. 490–491)
**20.** Explain how amino acids and proteins are reabsorbed. (p. 491)
**21.** Describe the effect of sodium reabsorption on the reabsorption of negatively charged ions. (p. 491)
**22.** Explain how sodium reabsorption affects water reabsorption. (p. 491)
**23.** Explain how potassium ions may be secreted passively. (p. 492)

**24.** The major action of ADH in the kidneys is to: (p. 493)
  a. increase water absorption by the proximal convoluted tubule.
  b. increase glomerular filtration rate.
  c. increase water reabsorption by the collecting duct.
  d. increase potassium's excretion.

**25.** Compare the processes that reabsorb urea and uric acid. (p. 493)

**26.** List the common constituents of urine and their sources. (p. 494)

**27.** Identify some of the factors that affect the volume of urine produced daily. (p. 494)

### 17.4 Urine Elimination

**28.** Describe the structure and function of a ureter. (p. 495)

**29.** Explain how the muscular wall of the ureter helps move urine. (p. 495)

**30.** Describe the structure and location of the urinary bladder. (p. 495)

**31.** Define *detrusor muscle*. (p. 495)

**32.** Distinguish between the internal and external urethral sphincters. (pp. 495–496)

**33.** Describe the micturition reflex. (p. 496)

**34.** Which of the following involves skeletal muscle? (p. 497).
  a. contraction of the internal urethral sphincter
  b. contraction of the external urethral sphincter
  c. ureteral peristalsis
  d. detrusor muscle contraction

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 3.3, 17.1, 17.2, 17.3

1. Imagine you are adrift at sea. Why will you dehydrate more quickly if you drink seawater instead of fresh water to quench your thirst?
2. Why are people following high-protein diets advised to drink large volumes of water?

### OUTCOMES 13.5, 17.2, 17.3

3. If blood pressure plummets in a patient in shock as a result of a severe injury, how would you expect urine production to change? Why?

### OUTCOMES 17.2, 17.3

4. Why may protein in the urine be a sign of kidney damage? What structures in the kidney are probably affected?
5. An infant is born with narrowed renal arteries. What effect will this condition have on urine volume?

### OUTCOMES 17.2, 17.4

6. Why do urinary tract infections frequently accompany sexually transmitted diseases?

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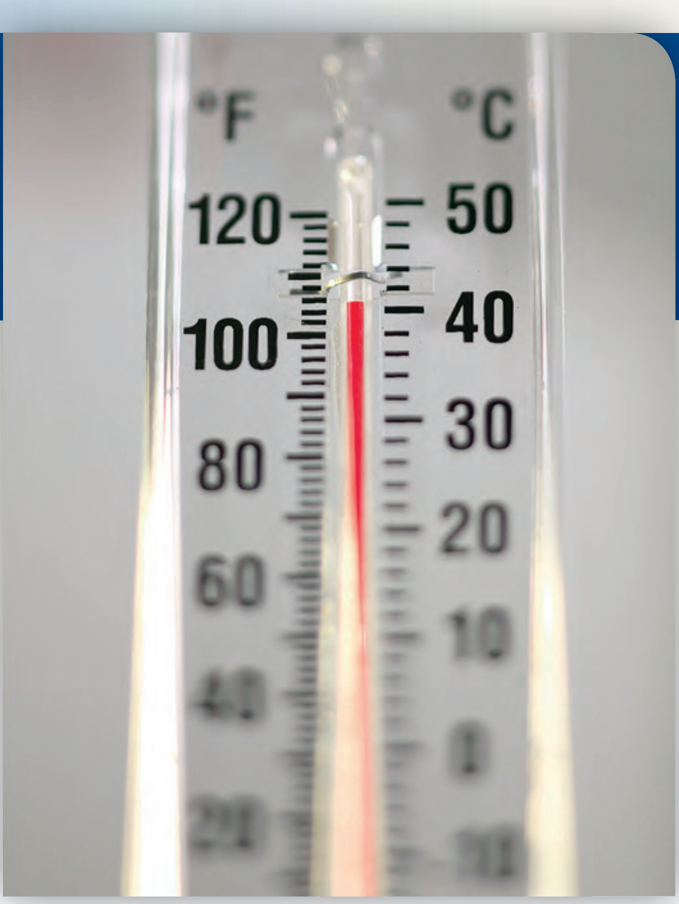
# 18

# Water, Electrolyte, and Acid-Base Balance



*An extremely high environmental temperature can challenge the body's ability to maintain a normal body temperature.*

Heatstroke can kill. Heatstroke, a form of hyperthermia, is a result of exposure to extreme environmental heat combined with a failure of normal body temperature control that can be quickly fatal. It occurs when the body is exposed to a heat index (heat considering humidity) of more than 105°F and body temperature reaches 104°F. Under these conditions, evaporation of sweat becomes less efficient at cooling the body, and organs begin to fail.

The symptoms of heatstroke happen in a sequence. First come headache, dizziness, and exhaustion. Sweating is profuse, then stops, as the skin becomes dry, hot, and red. Respiratory rate rises, and the pulse may race up to 180 beats per minute. If the person isn't cooled with fluids, water applied to the skin, fanning, and removal of clothing, neurological symptoms may begin. These include disorientation, hallucinations, and odd behavior. Kidney failure and/or heart arrhythmia may prove fatal.

During heat waves, the very young and the very old are more susceptible to heatstroke because their body temperature control mechanisms may be compromised. However, heatstroke also affects two groups of young, otherwise healthy individuals—athletes who work out in extreme heat and soldiers deployed to hot climates. In the Persian Gulf in July, the temperatures may soar to 122°F at midday, dipping down only to about 100°F at night. Some cases of unexpected sudden death in soldiers in Iraq and Afghanistan were due to heatstroke. For this reason, military officials insist that soldiers carry drinking water with them at all times and drink throughout the day, whether they feel thirsty or not.

Military researchers are conducting experiments to better understand the conditions under which heatstroke occurs. They are looking for biomarkers (see Clinical Application 2.2, page 57) to identify particularly susceptible individuals and to determine when it is safe for a soldier who has suffered a heat injury to return to battle.

Researchers in Israel are investigating gender differences in the response to heat stress. Past studies have shown that women begin to sweat at higher environmental temperatures than do men, but that in women sweat evaporates for a longer proportion of total sweat time than in men. The menstrual cycle also affects women's ability to withstand extreme heat. A woman is more susceptible to heatstroke during the second half of the menstrual cycle, when the hormone progesterone is at higher levels and the core body temperature is higher. One study is investigating thirty young women subjected to high heat and humidity while walking on a treadmill in a laboratory setup called a "climatic chamber." Each woman is being tested at two points in the menstrual cycle, and the researchers are assessing heart rate, core (rectal) temperature, skin temperature (chest, upper limb, lower limb), and fluid balance. The data will be compared with readings on young men, and the results will be used to protect soldiers of both genders from heatstroke.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

**18.1 Introduction**

1. Explain water and electrolyte balance. (p. 503)

**18.2 Distribution of Body Fluids**

2. Describe how body fluids are distributed in compartments. (pp. 503–504)

**18.3 Water Balance**

3. List the routes by which water enters and leaves the body, and explain how water intake and output are regulated. (pp. 505 and 508)

**18.4 Electrolyte Balance**

**4.** List the routes by which electrolytes enter and leave the body, and explain how electrolyte intake and output are regulated. (pp. 508–509)

**18.5 Acid-Base Balance**

**5.** List the major sources of hydrogen ions in the body. (p. 509)

**6.** Distinguish between strong and weak acids and bases. (p. 510)

**7.** Explain how chemical buffer systems, the respiratory center, and the kidneys keep the pH of body fluids relatively constant. (pp. 510–512)

**18.6 Acid-Base Imbalances**

**8.** Describe the causes and consequences of increase or decrease in body fluid pH. (pp. 512–515)

## AIDS TO UNDERSTANDING WORDS

*(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**de-** [separation from] *de*hydration: Removal of water from the cells or body fluids.

**extra-** [outside] *extra*cellular fluid: Fluid outside of the body cells.

**im-** [not] *im*balance: Condition in which factors are not in equilibrium.

**intra-** [within] *intra*cellular fluid: Fluid in body cells.

**neutr-** [neither one nor the other] *neutr*al: Solution that is neither acidic nor basic.

## 18.1 | Introduction

Two types of substances that are important in maintaining homeostasis in the body are water and **electrolytes,** which are molecules that release ions in water. To maintain homeostasis, water and electrolytes must be in balance; that is, the quantities entering the body must equal the quantities leaving it. Therefore, the body requires mechanisms to (1) replace lost water and electrolytes, and (2) excrete any excess.

Water balance and electrolyte balance are interdependent because electrolytes are dissolved in the water of body fluids. Consequently, anything that alters the concentrations of the electrolytes will alter the concentration of the water either by adding solutes to it or by removing solutes from it. Likewise, anything that changes the concentration of water will change concentrations of the electrolytes by concentrating or diluting them.

**PRACTICE**

1. How are water and electrolyte balance interdependent?

**FACTS OF LIFE** A human being is 60% water by weight. Losing one-fifth of that water volume can be fatal.

## 18.2 | Distribution of Body Fluids

Body fluids are not uniformly distributed. Instead, they occupy regions, or *compartments,* of different volumes that contain fluids of varying compositions. The movement of water and electrolytes between these compartments is regulated to stabilize both the distribution and the composition of body fluids.

### Fluid Compartments

The body of an average adult female is about 52% water by weight, and that of an average male is about 63% water. The reason for this difference is that females

CAREER CORNER

### Medical Laboratory Technician

A story lies behind every patient sample, and that's what the medical laboratory technician loves about her job. She analyzes specimens of blood, urine, saliva, and other body fluids or tissues to assist physicians in diagnosing disease. The urine sample before her now has tested positive for protein, an indication that the kidneys are not filtering normally. This is consistent with depressed levels of the protein albumin measured in the patient's blood, and with the accumulation of fluid in the patient's tissues, called edema.

A medical laboratory technician follows a patient sample as it is analyzed, conducting automated tests as well as observing cells under a microscope.

Medical laboratory technicians work in hospital labs, physicians' offices, diagnostic laboratories, forensics laboratories, and pharmaceutical and biotechnology companies.

Training varies. Many medical laboratory technicians earn associates degrees. Hospitals, technical programs, and the military also provide training. Education must include a clinical component, and the medical laboratory technician must pass a national certification exam.

generally have more adipose tissue, which contains little water. Males generally have more muscle tissue, which contains a great deal of water. Water in the adult human body (about 40 liters), with its dissolved electrolytes, is distributed into two major compartments: an intracellular fluid compartment and an extracellular fluid compartment.

The **intracellular** (in″trah-sel′u-lar) **fluid compartment** includes all the water and electrolytes that cell membranes enclose. In other words, intracellular fluid is the fluid inside cells, and in an adult it accounts for about 63% by volume of total body water.

The **extracellular** (ek″strah-sel′u-lar) **fluid compartment** includes all the fluid outside of cells—in tissue spaces (interstitial fluid), blood vessels (plasma), and lymphatic vessels (lymph). **Transcellular** (trans-sel′u-lar) **fluid**, a type of extracellular fluid, is found in cavities separated from other extracellular fluids by epithelial or connective tissue membranes. Transcellular fluid includes *cerebrospinal fluid* of the central nervous system, *aqueous* and *vitreous humors* of the eyes, *synovial fluid* of the joints, *serous fluid* in the body cavities, and fluid *secretions* of the exocrine glands. The fluids of the extracellular compartment constitute about 37% by volume of total body water (fig. 18.1).

## Body Fluid Composition

*Extracellular fluids* generally are similar in composition, including high concentrations of sodium, chloride, calcium, and bicarbonate ions and lesser concentrations of potassium, magnesium, phosphate, and sulfate ions. The blood plasma portion of extracellular fluid has considerably more protein than does either interstitial fluid or lymph.

*Intracellular fluid* has high concentrations of potassium, phosphate, and magnesium ions. It includes a greater concentration of sulfate ions and lesser concentrations of sodium, chloride, calcium, and bicarbonate ions than does extracellular fluid. Intracellular fluid also has a greater concentration of protein than plasma. Figure 18.2 shows these relative concentrations.

### PRACTICE

2. Describe the normal distribution of water in the body.
3. Which electrolytes are in higher concentrations in extracellular fluids? In intracellular fluid?
4. How does protein concentration vary in body fluids?

## Movement of Fluid Between Compartments

Two major factors regulate the movement of water and electrolytes from one fluid compartment to another: *hydrostatic pressure* and *osmotic pressure* (fig. 18.3). For example, as explained in chapter 13 (p. 367), fluid leaves the plasma at the arteriolar ends of capillaries and enters the interstitial spaces because of the net outward force of hydrostatic pressure (blood pressure). Fluid returns to the plasma from the interstitial spaces at the venular ends of capillaries because of the net inward force of *colloid osmotic pressure* due to the plasma proteins. Likewise, as chapter 14 mentioned (p. 389), fluid leaves the interstitial spaces and enters the lymph capillaries due to the hydrostatic pressure of the interstitial fluid. The circulation of lymph returns interstitial fluid to the plasma.

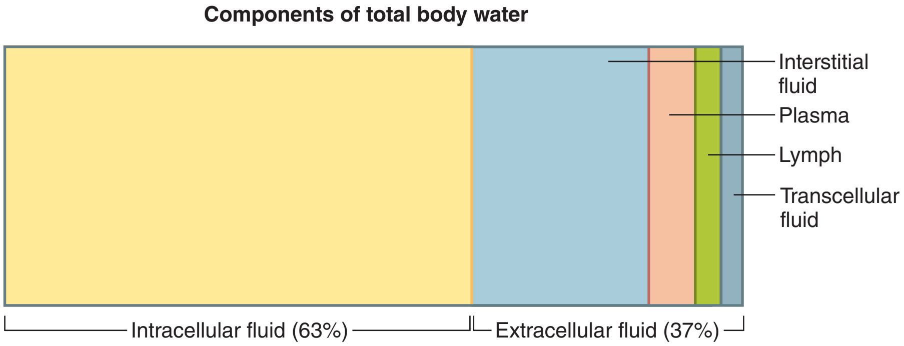
Hydrostatic pressure within the cells and surrounding interstitial fluid is ordinarily equal and remains stable. Therefore, any net fluid movement is likely to be the result of changes in osmotic pressure.

The total solute concentration in extracellular and intracellular fluids is normally equal. A decrease in extracellular sodium ion concentration causes a net movement of water from the extracellular compartment into the intracellular compartment by osmosis. The cells swell. Conversely, if the extracellular sodium ion concentration increases, cells shrink as they lose water by osmosis.

### PRACTICE

5. Which factors control the movement of water and electrolytes from one fluid compartment to another?
6. How does the sodium ion concentration in body fluids affect the net movement of water between the compartments?

**FIGURE 18.1** Approximately two-thirds of the water in the body is inside cells.



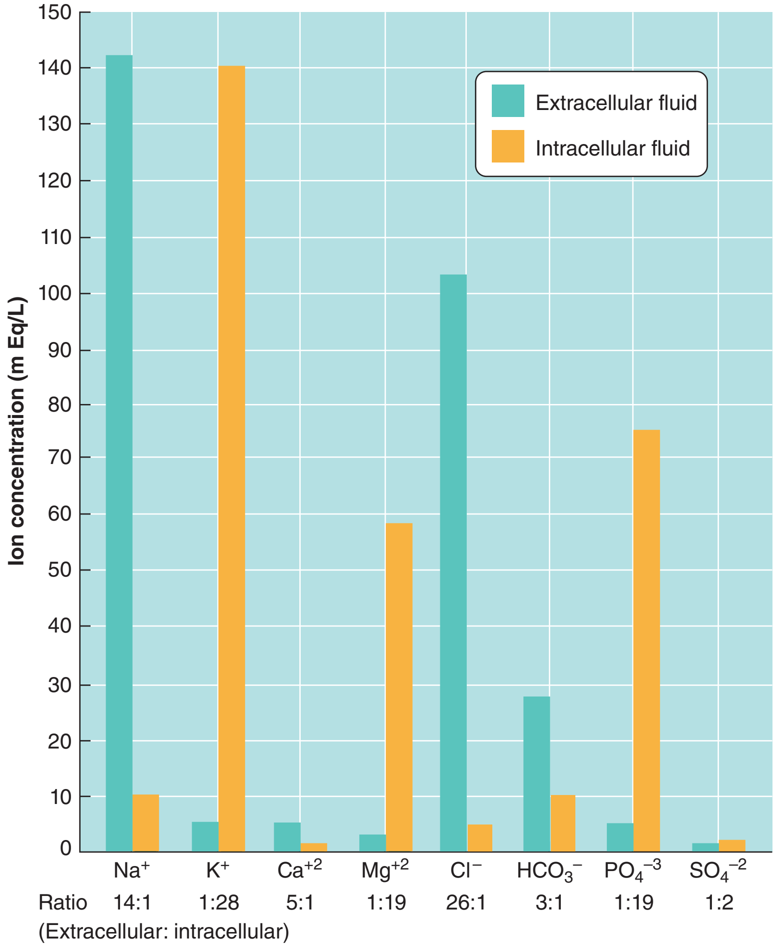


**FIGURE 18.2** Extracellular fluids have relatively high concentrations of sodium ($Na^+$), calcium ($Ca^{+2}$), chloride ($Cl^-$), and bicarbonate ($HCO_3^-$) ions. Intracellular fluid has relatively high concentrations of potassium ($K^+$), magnesium ($Mg^{+2}$), phosphate ($PO_4^{-3}$), and sulfate ($SO_4^{-2}$) ions.

Q *According to the graph, which positively charged intracellular fluid ion is in the highest concentration?*

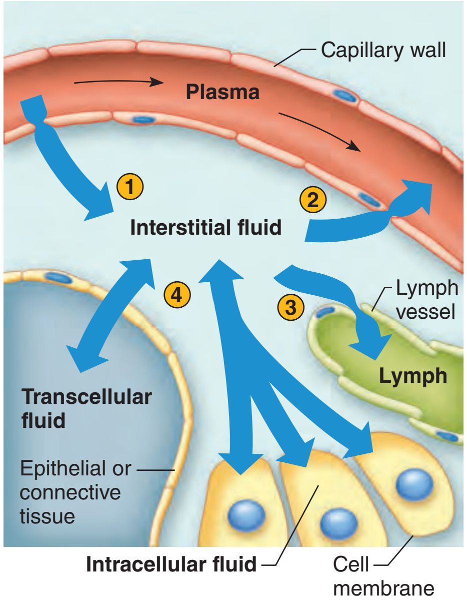
**Answer can be found in Appendix F on page 582.**

## 18.3 | Water Balance

**Water balance** exists when water intake equals water output. Homeostasis requires control of both water intake and water output. Clinical Application 18.1 discusses water balance disorders, including dehydration, edema, and water intoxication.

### Water Intake

The volume of water gained each day varies among individuals. An average adult living in a moderate environment takes in about 2,500 milliliters. Probably 60% is obtained from drinking water or beverages, and another 30% comes from moist foods. The remaining 10% is a by-product of the oxidative metabolism of nutrients (chapter 4, p. 91), called **water of metabolism** (fig. 18.4*a*).



① Fluid leaves plasma at arteriolar ends of capillaries because the outward force of hydrostatic pressure predominates

② Fluid returns to plasma at venular ends of the capillaries because the inward force of colloid osmotic pressure predominates

③ Hydrostatic pressure within interstitial spaces forces fluid into lymph capillaries

④ Interstitial fluid is in equilibrium with transcellular and intracellular fluids

**FIGURE 18.3** Net movements of fluids between compartments result from differences in hydrostatic and osmotic pressures.

The primary regulator of water intake is thirst. The intense feeling of thirst derives from the osmotic pressure of extracellular fluids and a *thirst center* in the hypothalamus of the brain. As the body loses water, the osmotic pressure of extracellular fluids increases. Such a change stimulates *osmoreceptors* in the thirst center, and in response, the hypothalamus causes the person to feel thirsty and to seek water.

Thirst is a homeostatic mechanism, normally triggered when total body water decreases by as little as 1%. Drinking distends the stomach wall, triggering impulses that inhibit the thirst mechanism. In this way, drinking stops even before the swallowed water is absorbed, preventing the person from drinking more than is required to replace the volume lost, avoiding development of an imbalance.

**PRACTICE**

7. What is water balance?
8. Where is the thirst center?
9. What stimulates fluid intake? What inhibits it?

### Water Output

Water normally enters the body only through the mouth, but it can be lost by a variety of routes. These include obvious losses in urine, feces, and sweat (sensible perspiration), as well as evaporation of water from

## CLINICAL APPLICATION 18.1

## Water Balance Disorders

Dehydration, water intoxication, and edema are among the more common disorders that involve a water imbalance in body fluids.

### Dehydration

In *dehydration,* water output exceeds water intake. Dehydration may develop following excessive sweating or as a result of prolonged water deprivation accompanied by continued water output. The extracellular fluid becomes more concentrated, and water leaves cells by osmosis (fig. 18A). Dehydration may also accompany prolonged vomiting or diarrhea that depletes body fluids.

During dehydration, the skin and mucous membranes of the mouth feel dry, and body weight drops. Severe hyperthermia may develop as the body's temperature-regulating mechanism falters due to lack of water for sweat.

Infants are more likely to become dehydrated because their kidneys are less efficient at conserving water than those of adults. Elderly people are also especially susceptible to developing water imbalances because the sensitivity of their thirst mechanism decreases with age, and physical disabilities may make it difficult for them to obtain adequate fluids.

The treatment for dehydration is to replace the lost water and electrolytes. If only water is replaced, the extracellular fluid will become more dilute than normal, causing cells to swell (fig. 18B). This may produce a condition called water intoxication.

### Water Intoxication

Until recently, runners were advised to drink as much fluid as they could, particularly in long events. But the death of a young woman in a marathon from low blood sodium (*hyponatremia*) due to excessive water intake leading to *water intoxication* inspired

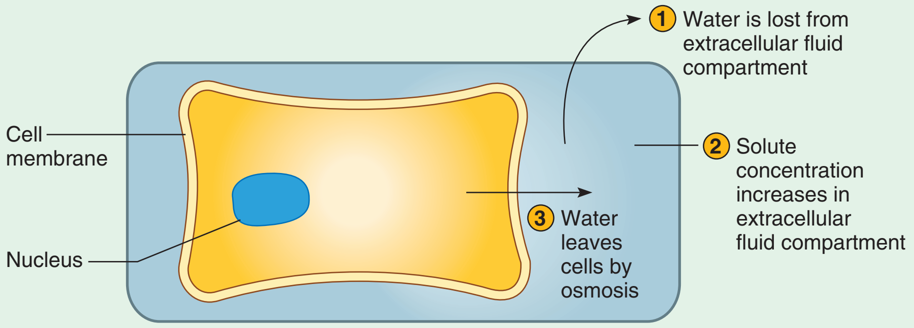

① Water is lost from extracellular fluid compartment
Cell membrane
② Solute concentration increases in extracellular fluid compartment
Nucleus
③ Water leaves cells by osmosis

**FIGURE 18A** If excess extracellular fluids are lost, cells dehydrate by osmosis.

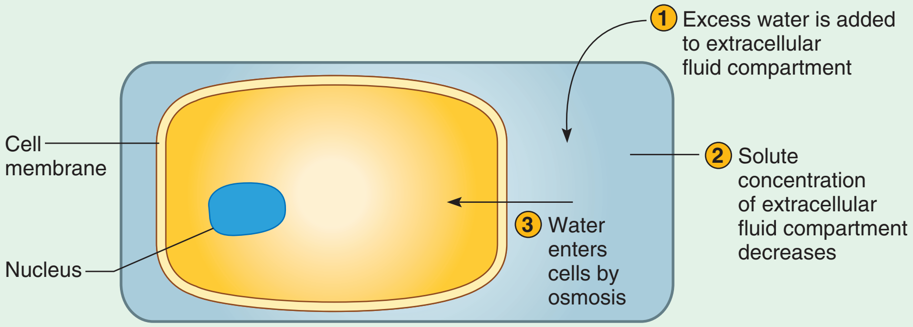

① Excess water is added to extracellular fluid compartment
Cell membrane
② Solute concentration of extracellular fluid compartment decreases
Nucleus
③ Water enters cells by osmosis

**FIGURE 18B** If excess water is added to the extracellular fluid compartment, cells gain water by osmosis.

further study and a reevaluation of this advice. Researchers from Harvard Medical School studied 488 runners from the race and found that 13% of them had developed hyponatremia. The tendency to develop the condition was associated with longer race time, high or low body mass index, and significant weight gain during the race. Drinking sports drinks instead of water does not make a difference because these beverages are mostly water.

In recognition of the possibility of hyponatremia, USA Track and Field, the national governing body for the sport, advises runners how to determine how much water to drink during a one-hour training run. The goal is to replace exactly what is lost.

## Edema

*Edema* is an abnormal accumulation of extracellular fluid in the interstitial spaces. Causes include a decrease in the plasma protein concentration (*hypoproteinemia*), obstructions in lymphatic vessels, increased venous pressure, and increased capillary permeability.

Hypoproteinemia may result from failure of the liver to synthesize plasma proteins; kidney disease that damages glomerular capillaries, allowing proteins to enter the urine; or starvation, in which amino acid intake is insufficient to support synthesis of plasma proteins. In each of these instances, the plasma protein concentration is decreased, which decreases plasma colloid osmotic pressure, reducing the normal return of tissue fluid to the venular ends of capillaries. Consequently, tissue fluid accumulates in the interstitial spaces.

Edema may result from *lymphatic obstructions* due to surgery or parasitic infections of lymphatic vessels, as discussed in chapter 14 (p. 391). Back pressure develops in the lymphatic vessels, which interferes with the normal movement of tissue fluid into them. At the same time, proteins that the lymphatic circulation ordinarily removes accumulate in interstitial spaces, raising the osmotic pressure of interstitial fluid. This effect draws still more fluid into the interstitial spaces.

If blood outflow from the liver into the inferior vena cava is blocked, the venous pressure in the liver and portal blood vessels greatly increases. As a result, fluid with a high protein concentration is exuded from the surfaces of the liver and intestine into the peritoneal cavity. The protein buildup elevates the osmotic pressure of the abdominal fluid, which in turn draws more water into the peritoneal cavity by osmosis, causing the painful condition *ascites*.

Edema may also result from increased capillary permeability accompanying *inflammation*. Recall that inflammation is a response to tissue damage and usually releases chemicals such as histamine from damaged cells. Histamine causes vasodilation and increased capillary permeability. As a result, excess fluid leaks out of the capillary and enters the interstitial spaces. Table 18A summarizes the factors that result in edema.

**TABLE 18A Factors Associated with Edema**

| Factor | Cause | Effect |
|---|---|---|
| Low plasma protein concentration | Liver disease and failure to synthesize proteins; kidney disease and loss of proteins in urine; lack of proteins in diet due to starvation | Plasma colloid osmotic pressure decreases; less fluid reabsorbed at venular ends of capillaries by osmosis |
| Obstruction of lymphatic vessels | Surgical removal of portions of lymphatic pathways; certain parasitic infections | Back pressure in lymph vessels interferes with movement of fluid from interstitial spaces into lymph capillaries |
| Increased venous pressure | Venous obstructions or faulty venous valves | Back pressure in veins increases capillary filtration |
| Inflammation | Tissue damage | Vasodilation and increased capillary permeability lead to increased filtration |

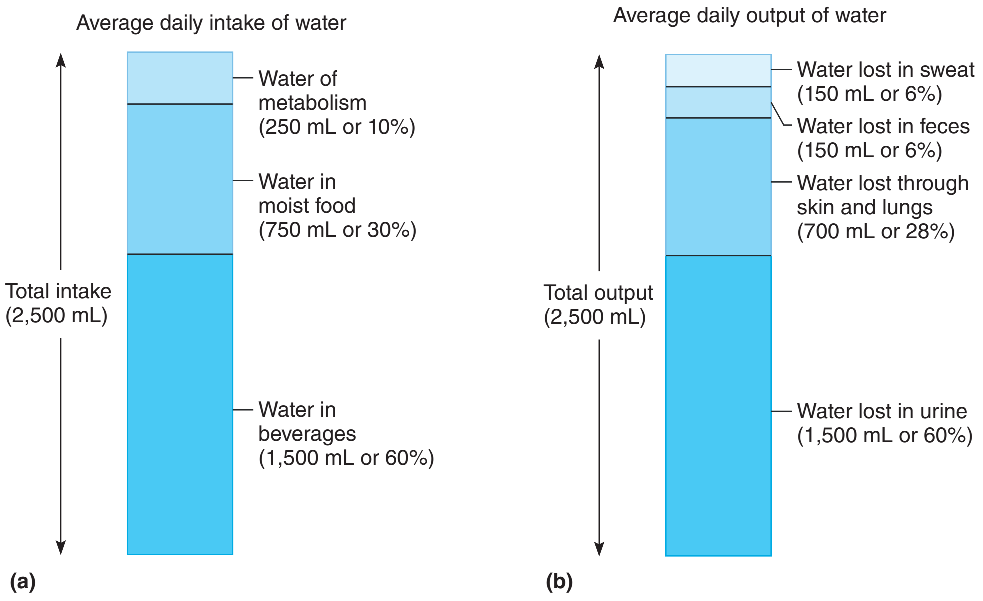


**FIGURE 18.4** Water balance. **(a)** Major sources of body water. **(b)** Routes by which the body loses water.

the skin (insensible perspiration) and from the lungs during breathing.

If an average adult takes in 2,500 milliliters of water each day, then 2,500 milliliters must be eliminated to maintain water balance. Of this volume, perhaps 60% is lost in urine, 6% in feces, and 6% in sweat. About 28% is lost by evaporation from the skin and lungs (fig. 18.4*b*). These percentages vary with such environmental factors as temperature and relative humidity and with physical exercise.

The primary means of regulating water output is urine production. The renal distal convoluted tubules of the nephrons and collecting ducts are the effectors of the mechanism that regulates urine volume. The epithelial linings in these structures remain relatively impermeable to water unless antidiuretic hormone (ADH) is present. ADH increases the permeability of the distal convoluted tubule and collecting duct, thereby increasing water reabsorption and reducing urine production. In the absence of ADH, less water is reabsorbed and more urine is produced (see chapter 17, p. 493).

*Diuretics* are chemicals that promote urine production. They act in different ways. Alcohol and certain narcotic drugs promote urine formation by inhibiting ADH release. A drug called mannitol is an osmotic diuretic. It is filtered by the kidneys, but is not reabsorbed, so it draws water into the renal tubules by osmosis and more water is lost in the urine. Mannitol is used in some patients to increase urinary excretion of toxins. It is also used to sweeten gum, but not in sufficient amounts to have a diuretic effect.

**PRACTICE**

10. By what routes does the body lose water?
11. What is the primary regulator of water loss?

## 18.4 | Electrolyte Balance

**Electrolyte balance** exists when the quantities of electrolytes the body gains equal those lost. Homeostatic mechanisms maintain electrolyte balance.

### Electrolyte Intake

The electrolytes of greatest importance to cellular functions dissociate to release sodium, potassium, calcium, magnesium, chloride, sulfate, phosphate, bicarbonate, and hydrogen ions. These electrolytes are primarily obtained from foods, but they may also be found in drinking water and other beverages. In addition, some electrolytes are by-products of metabolic reactions.

Ordinarily, a person obtains sufficient electrolytes by responding to hunger and thirst. However, a severe electrolyte deficiency may cause *salt craving,* which is a strong desire to eat salty foods.

### Electrolyte Output

The body loses some electrolytes by perspiring, with more lost in sweat on warmer days and during strenuous exercise. Varying amounts of electrolytes are lost in the feces. The greatest electrolyte output is a result of kidney function and urine production. The kidneys alter electrolyte output to maintain the proper composition of body fluids, thereby promoting homeostasis.

### PRACTICE

12. Which electrolytes are most important to cellular functions?
13. Which mechanisms ordinarily regulate electrolyte intake?
14. By what routes does the body lose electrolytes?

---

Precise concentrations of positively charged ions, such as sodium ($Na^+$), potassium ($K^+$), and calcium ($Ca^{+2}$), are required for impulse conduction along an axon, muscle fiber contraction, and maintenance of cell membrane potential. *Sodium ions* account for nearly 90% of positively charged ions in extracellular fluids. The kidneys and the hormone aldosterone regulate these ions. Aldosterone, which the adrenal cortex secretes, increases sodium ion reabsorption in the distal convoluted tubules of the kidneys' nephrons and in the collecting ducts.

Aldosterone also regulates potassium ions. A rising potassium ion concentration directly stimulates cells of the adrenal cortex to secrete aldosterone. This hormone enhances tubular secretion of potassium ions at the same time that it causes tubular reabsorption of sodium ions (fig. 18.5). Clinical Application 18.2 discusses conditions resulting from an imbalance of sodium and potassium ions.

Recall from chapter 11 (pp. 312–313) that the calcium ion concentration dropping below normal directly stimulates the parathyroid glands to secrete parathyroid hormone. This hormone returns the concentration of calcium in extracellular fluids toward normal.

Generally the regulatory mechanisms that control positively charged ions secondarily control the concentrations of negatively charged ions. For example, chloride ions ($Cl^-$), the most abundant negatively charged ions in extracellular fluids, are passively reabsorbed in response to the active tubular reabsorption of sodium ions. That is, the negatively charged chloride ions are electrically attracted to positively charged sodium ions and accompany them as they are reabsorbed (see chapter 17, p. 491).

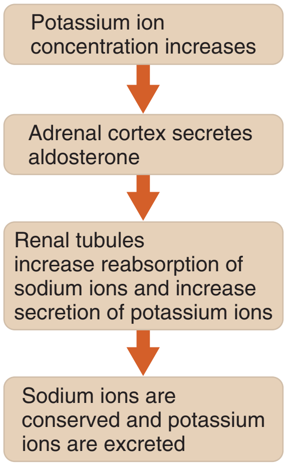

Potassium ion concentration increases
Adrenal cortex secretes aldosterone
Renal tubules increase reabsorption of sodium ions and increase secretion of potassium ions
Sodium ions are conserved and potassium ions are excreted

**FIGURE 18.5** If the potassium ion concentration increases, the kidneys conserve sodium ions and excrete potassium ions.

Active transport mechanisms with limited transport capacities partially regulate some negatively charged ions, such as phosphate ions ($PO_4^{-3}$) and sulfate ions ($SO_4^{-2}$). Therefore, if the extracellular phosphate ion concentration is low, renal tubules reabsorb phosphate ions. On the other hand, if the renal plasma threshold is exceeded, excess phosphate is excreted in urine.

### PRACTICE

15. How does aldosterone regulate sodium and potassium ion concentration?
16. How is calcium regulated?
17. What mechanism regulates the concentrations of most negatively charged ions?

---

## 18.5 | Acid-Base Balance

Electrolytes that release hydrogen ions are called **acids,** and electrolytes that release ions that combine with hydrogen ions are called **bases,** as chapter 2 discussed (p. 47). Maintenance of homeostasis depends on balancing the concentrations of acids and bases in body fluids.

### Sources of Hydrogen Ions

Most of the hydrogen ions in body fluids originate as by-products of metabolic processes, although the digestive tract may directly absorb some hydrogen ions. The major metabolic sources of hydrogen ions include the following (fig. 18.6):

1. **Aerobic respiration of glucose** This process produces carbon dioxide and water. Carbon dioxide diffuses out of the cells and reacts with the water in the extracellular fluids to form *carbonic acid,* which then ionizes to release hydrogen ions and bicarbonate ions:

$$H_2CO_3 \longrightarrow H^+ + HCO_3^-$$

2. **Anaerobic respiration of glucose** Anaerobically metabolized glucose produces *lactic acid,* which adds hydrogen ions to body fluids.
3. **Incomplete oxidation of fatty acids** This process produces *acidic ketone bodies,* which increase hydrogen ion concentration.
4. **Oxidation of amino acids containing sulfur** This process yields *sulfuric acid* ($H_2SO_4$), which ionizes to release hydrogen ions.

CLINICAL APPLICATION **18.2**

### Sodium and Potassium Imbalances

Extracellular fluids usually have high sodium ion concentrations, and intracellular fluid usually has a high potassium ion concentration. Renal regulation of sodium is closely related to that of potassium, because active reabsorption of sodium (under the influence of aldosterone) is accompanied by tubular secretion (and excretion) of potassium. Therefore, conditions resulting from sodium ion imbalance often also involve potassium ion imbalance.

Such disorders include:

1. *Low blood sodium concentration (hyponatremia)* Possible causes of sodium deficiencies include prolonged sweating, vomiting, or diarrhea; renal disease in which sodium is inadequately reabsorbed; adrenal cortex disorders in which aldosterone secretion is insufficient to promote sodium reabsorption (Addison disease); and drinking too much water. One possible effect of hyponatremia is the development of hypotonic extracellular fluid that promotes water movement into cells by osmosis, producing symptoms of water intoxication.
2. *High blood sodium concentration (hypernatremia)* Possible causes of elevated sodium concentration include excessive water loss by evaporation (despite decreased sweating, as may occur during high fever), or increased water loss accompanying diabetes insipidus. In one form of diabetes insipidus, the secretion of antidiuretic hormone (ADH) is insufficient for the renal tubules and collecting ducts to conserve water. Hypernatremia may disturb the central nervous system, causing confusion, stupor, and coma.
3. *Low blood potassium concentration (hypokalemia)* Possible causes of potassium deficiency include the release of excess aldosterone by the adrenal cortex (Cushing syndrome), which increases renal excretion of potassium; use of diuretic drugs that promote potassium excretion; kidney disease; and prolonged vomiting or diarrhea. Possible effects of hypokalemia include muscular weakness or paralysis, respiratory difficulty, and severe cardiac disturbances, such as atrial or ventricular arrhythmias.
4. *High blood potassium concentration (hyperkalemia)* Possible causes of elevated potassium concentration include renal disease, which decreases potassium excretion; use of drugs that promote renal conservation of potassium; the release of insufficient aldosterone by the adrenal cortex (Addison disease); or a shift of potassium from the intracellular to the extracellular fluid, a change that accompanies an increase in plasma hydrogen ion concentration (acidosis). Possible effects of hyperkalemia include paralysis of the skeletal muscles and severe cardiac disturbances, such as cardiac arrest.

5. **Breakdown (hydrolysis) of phosphoproteins and nucleic acids** Phosphoproteins and nucleic acids contain phosphorus. Their oxidation produces *phosphoric acid* ($H_3PO_4$), which ionizes to release hydrogen ions.

The acids resulting from metabolism vary in strength. Therefore, their effects on the hydrogen ion concentration of body fluids vary.

**PRACTICE**

18. Distinguish between an acid and a base.
19. What are the major sources of hydrogen ions in the body?

## Strengths of Acids and Bases

Acids that ionize more completely are *strong acids,* and those that ionize less completely are *weak acids.* For example, the hydrochloric acid (HCl) of gastric juice is a strong acid, but the carbonic acid ($H_2CO_3$) produced when carbon dioxide reacts with water is weak.

Bases release ions, such as hydroxide ions ($OH^-$), which can combine with hydrogen ions, thereby lowering their concentration. Sodium hydroxide (NaOH), which releases hydroxide ions, and sodium bicarbonate ($NaHCO_3$), which releases bicarbonate ions ($HCO_3^-$), are bases. Strong bases dissociate to release more $OH^-$ or its equivalent than do weak bases. Often the negative ions themselves are called bases. For example, $HCO_3^-$ acting as a base combines with $H^+$ from the strong acid HCl to form the weak acid carbonic acid ($H_2CO_3$).

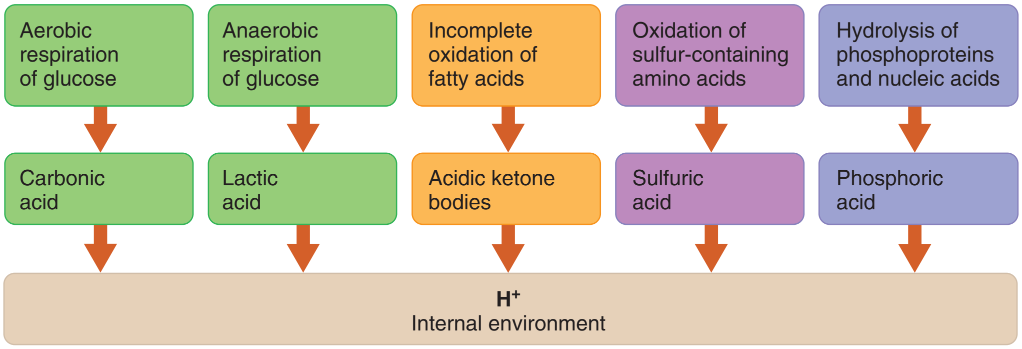
## Regulation of Hydrogen Ion Concentration

Chemical buffer systems, the respiratory center in the brainstem, and the nephrons in the kidneys regulate hydrogen ion concentration in body fluids. The pH scale is used to measure hydrogen ion concentration.

### *Chemical Buffer Systems*

**Chemical buffer systems,** in all body fluids, consist of chemicals that combine with excess acids or bases. More specifically, the chemical components of a buffer system can combine with strong acids to convert them into weak

**FIGURE 18.6** Some of the metabolic processes that provide hydrogen ions.


Aerobic respiration of glucose
Anaerobic respiration of glucose
Incomplete oxidation of fatty acids
Oxidation of sulfur-containing amino acids
Hydrolysis of phosphoproteins and nucleic acids
Carbonic acid
Lactic acid
Acidic ketone bodies
Sulfuric acid
Phosphoric acid
H+
Internal environment

acids. Likewise, these buffers can combine with strong bases to convert them into weak bases. Such reactions help minimize pH changes in body fluids. The three most important chemical buffer systems in body fluids are:

1. **Bicarbonate buffer system** The bicarbonate buffer system, which is present in both intracellular and extracellular fluids, uses the bicarbonate ion ($HCO_3^-$), acting as a weak base, and carbonic acid ($H_2CO_3$), acting as a weak acid. In the presence of excess hydrogen ions, bicarbonate ions combine with hydrogen ions to form carbonic acid, thereby minimizing any increase in the hydrogen ion concentration of the body fluids:

   $$H^+ + HCO_3^- \longrightarrow H_2CO_3$$

   On the other hand, if conditions are basic or alkaline, carbonic acid dissociates to release bicarbonate ions and hydrogen ions:

   $$H_2CO_3 \longrightarrow H^+ + HCO_3^-$$

   Although this reaction releases bicarbonate ions, it is the increase of free hydrogen ions at equilibrium that is important in minimizing the shift toward a more alkaline pH.
2. **Phosphate buffer system** The phosphate buffer system also operates in both intracellular and extracellular body fluids. However, it is particularly important in the control of hydrogen ion concentrations in the tubular fluid of the nephrons and in urine. This buffer system consists of two phosphate ions, monohydrogen phosphate ($HPO_4^{-2}$), acting as a weak base, and dihydrogen phosphate ($H_2PO_4^-$), acting as a weak acid. In the presence of excess hydrogen ions, monohydrogen phosphate ions combine with hydrogen ions to form dihydrogen phosphate, thereby minimizing the increase in the hydrogen ion concentration of body fluids:

   $$H^+ + HPO_4^{-2} \longrightarrow H_2PO_4^-$$

   On the other hand, if conditions are basic or alkaline, dihydrogen phosphate dissociates to release monohydrogen phosphate and hydrogen ions:

   $$H_2PO_4^- \longrightarrow H^+ + HPO_4^{-2}$$
3. **Protein buffer system** The protein buffer system consists of the plasma proteins, such as albumins, and certain proteins in cells, including the hemoglobin of red blood cells. As described in chapter 2 (pp. 53–55), proteins are chains of amino acids. Some of these amino acids have freely exposed amino groups ($-NH_2$). If the solution pH falls (hydrogen ion concentration rises), these amino groups can accept hydrogen ions:

   $$-NH_2 + H^+ \longrightarrow -NH_3^+$$

   Some amino acids of a protein also have freely exposed *carboxyl groups* ($-COOH$). If the solution pH rises (hydrogen ion concentration falls), these carboxyl groups can ionize, releasing hydrogen ions:

   $$-COOH \longrightarrow -COO^- + H^+$$

   Therefore, protein molecules can function as bases by accepting hydrogen ions into their amino groups or as acids by releasing hydrogen ions from their carboxyl groups. This special property allows protein molecules to operate as an acid-base buffer system, minimizing changes in pH.

Table 18.1 summarizes the actions of the three major chemical buffer systems.

Neurons are particularly sensitive to changes in the pH of body fluids. If the interstitial fluid becomes more alkaline than normal, neurons become more excitable and seizures may result. Conversely, acidic conditions depress neuron activity, and may reduce the level of consciousness.

## PRACTICE

20. What is the difference between a strong acid or base and a weak acid or base?
21. How does a chemical buffer system help regulate the pH of body fluids?
22. List the major chemical buffer systems of the body.

**TABLE 18.1 Chemical Buffer Systems**

| Buffer System | Constituents | Actions |
|---|---|---|
| Bicarbonate system | Bicarbonate ion ($HCO_3^-$) | Combines with a hydrogen ion in the presence of excess acid |
| | Carbonic acid ($H_2CO_3$) | Releases a hydrogen ion in the presence of excess base |
| Phosphate system | Monohydrogen phosphate ion ($HPO_4^{-2}$) | Combines with a hydrogen ion in the presence of excess acid |
| | Dihydrogen phosphate ion ($H_2PO_4^-$) | Releases a hydrogen ion in the presence of excess base |
| Protein system (and amino acids) | $-NH_2$ group of an amino acid or protein | Combines with a hydrogen ion in the presence of excess acid |
| | $-COOH$ group of an amino acid or protein | Releases a hydrogen ion in the presence of excess base |

### *Respiratory Excretion of Carbon Dioxide*

The respiratory center in the brainstem helps regulate the hydrogen ion concentrations in the body fluids by controlling the rate and depth of breathing (see chapter 16, pp. 468–469). Figure 18.7 traces this process. Specifically, if body cells increase their production of carbon dioxide, as occurs during periods of physical exertion, carbonic acid production increases. As the carbonic acid dissociates, the concentration of hydrogen ions increases, and the pH of the internal environment drops. Such an increasing concentration of carbon dioxide in the central nervous system and the subsequent increase in hydrogen ion concentration in the cerebrospinal fluid stimulate chemosensitive areas in the respiratory center.

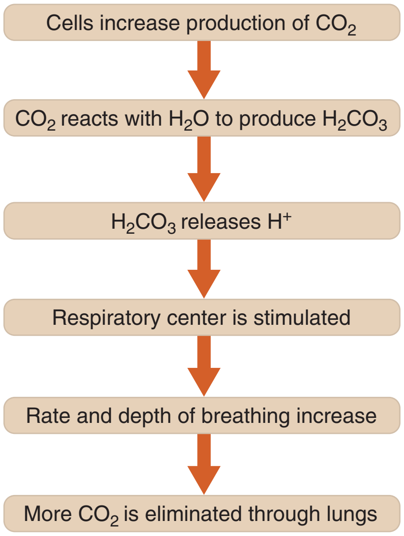

Cells increase production of $CO_2$
$CO_2$ reacts with $H_2O$ to produce $H_2CO_3$
$H_2CO_3$ releases $H^+$
Respiratory center is stimulated
Rate and depth of breathing increase
More $CO_2$ is eliminated through lungs

**FIGURE 18.7** An increase in carbon dioxide production increases carbon dioxide elimination.

In response, the respiratory center increases the depth and rate of breathing, so that the lungs excrete more carbon dioxide. Hydrogen ion concentration in body fluids returns toward normal because the released carbon dioxide comes from carbonic acid:

$$H_2CO_3 \longrightarrow CO_2 + H_2O$$

Conversely, if body cells are less active, concentrations of carbon dioxide and hydrogen ions in body fluids remain low. As a result, breathing rate and depth stay closer to resting levels.

### *Renal Excretion of Hydrogen Ions*

Nephrons help regulate the hydrogen ion concentration of body fluids by excreting hydrogen ions in urine. Recall from chapter 17 (p. 492) that epithelial cells lining certain segments of the renal tubules secrete hydrogen ions into the tubular fluid.

### *Time Course of Hydrogen Ion Regulation*

The various regulators of hydrogen ion concentration operate at different rates. Chemical buffers can convert strong acids or bases into weak acids or bases almost immediately. For this reason, these chemical buffer systems are called the body's *first line of defense* against shifts in pH.

Physiological buffer systems, such as the respiratory and renal mechanisms, function more slowly and constitute the *second line of defense* against shifts in pH. The respiratory mechanism may require several minutes to begin resisting a change in pH, and the renal mechanism may require one to three days to regulate a changing hydrogen ion concentration. Figure 18.8 compares the actions of chemical buffers and physiological buffers.

**PRACTICE**

23. How does the respiratory system help regulate acid-base balance?
24. How do the kidneys respond to excess hydrogen ions?
25. How do the rates at which chemical and physiological buffer systems act differ?

## 18.6 | Acid-Base Imbalances

Chemical and physiological buffer systems ordinarily maintain the hydrogen ion concentration of body fluids within very narrow pH ranges. Abnormal conditions may disturb the acid-base balance. For example, the pH of arterial blood is normally 7.35–7.45. A pH value

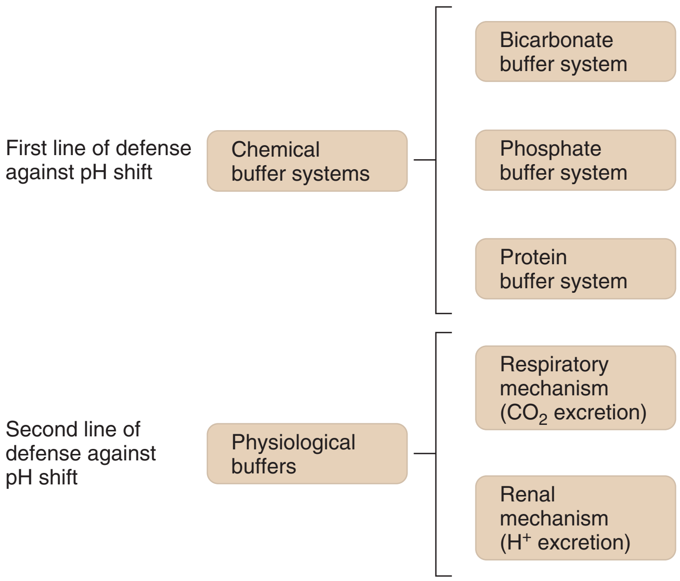

First line of defense against pH shift
Chemical buffer systems
Bicarbonate buffer system
Phosphate buffer system
Protein buffer system
Second line of defense against pH shift
Physiological buffers
Respiratory mechanism ($CO_2$ excretion)
Renal mechanism ($H^+$ excretion)

**FIGURE 18.8** Chemical buffers act rapidly, whereas physiological buffers may require several minutes to several days to begin resisting a change in pH.

**Q** *How does respiratory excretion of $CO_2$ buffer the pH of body fluids?*

**Answer can be found in Appendix F on page 582.**

below 7.35 produces *acidosis.* A pH above 7.45 produces *alkalosis.* Such shifts in the pH of body fluids can be life-threatening. A person usually cannot survive if the pH drops to 6.8 or rises to 8.0 for more than a few hours (fig. 18.9).

Acidosis results from an accumulation of acids or loss of bases, both of which cause abnormal increases in the hydrogen ion concentrations of body fluids. Conversely, alkalosis results from a loss of acids or an accumulation of bases accompanied by a decrease in hydrogen ion concentrations (fig. 18.10).

## Acidosis

The two major types of acidosis are *respiratory acidosis* and *metabolic acidosis.* Factors that increase carbon dioxide levels, which increases the concentration of carbonic acid (the respiratory acid), cause respiratory acidosis. Metabolic acidosis is due to an abnormal accumulation of any other acids in the body fluids or to loss of bases, including bicarbonate ions.

Respiratory acidosis may be due to hindered pulmonary ventilation, which increases carbon dioxide concentration. This may result from the following conditions:

1. Injury to the respiratory center of the brainstem, decreasing rate and depth of breathing.

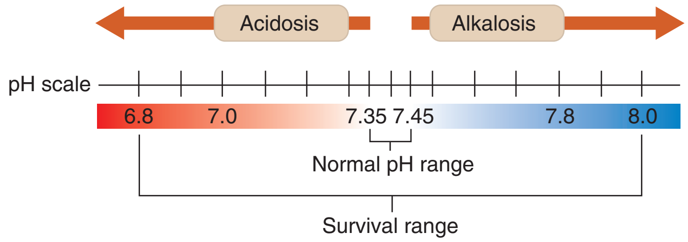

Acidosis
Alkalosis
pH scale
6.8
7.0
7.35
7.45
7.8
8.0
Normal pH range
Survival range

**FIGURE 18.9** If the pH of arterial blood drops to 6.8 or rises to 8.0 for more than a few hours, the person usually cannot survive.

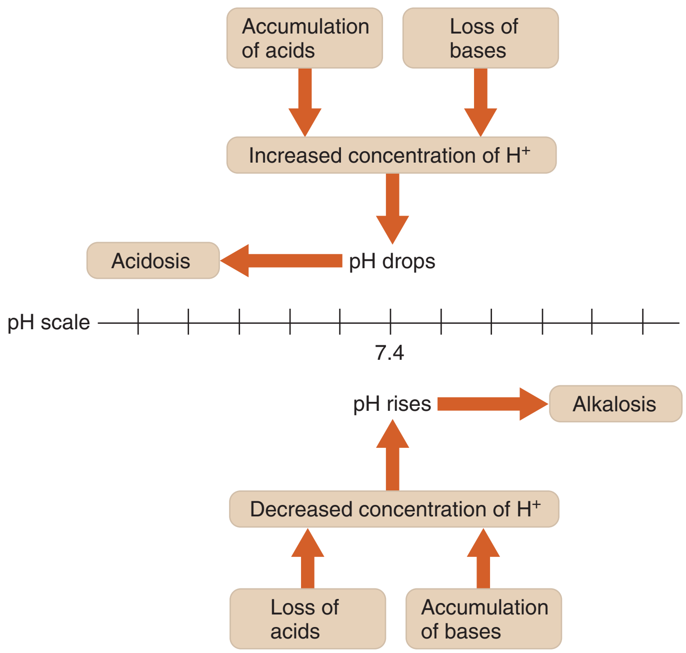

Accumulation of acids
Loss of bases
Increased concentration of $H^+$
pH drops
Acidosis
pH scale
7.4
pH rises
Alkalosis
Decreased concentration of $H^+$
Loss of acids
Accumulation of bases

**FIGURE 18.10** Acidosis results from accumulation of acids or loss of bases. Alkalosis results from loss of acids or accumulation of bases.

2. Obstruction in air passages that interferes with air movement into and out of the alveoli.
3. Diseases that decrease gas exchange, such as pneumonia, or those that reduce the surface area of the respiratory membrane, such as emphysema.

Figure 18.11 summarizes the factors that can lead to respiratory acidosis. Any of these conditions can increase the level of carbonic acid and hydrogen ions in body fluids, lowering pH. Chemical buffers, such as hemoglobin, may resist this shift in pH. At the same time, increasing levels of carbon dioxide and hydrogen ions stimulate the respiratory center, increasing the breathing rate and depth and thereby lowering the carbon dioxide levels. Also, the kidneys may begin to excrete more hydrogen ions. Eventually, these chemical and physiological buffers return the pH of the body fluids to normal. The acidosis is thus *compensated.*

Metabolic acidosis is due to either accumulation of nonrespiratory acids or loss of bases. Factors that may lead to this condition include the following:

1. Kidney disease that reduces glomerular filtration so that the kidneys fail to excrete acids produced in metabolism (uremic acidosis).
2. Prolonged vomiting that loses the alkaline contents of the upper intestine. (Losing only the stomach contents produces metabolic alkalosis. Vomiting can empty not only the stomach, but also the first foot or so of the intestine.)
3. Prolonged diarrhea in which excess alkaline intestinal secretions are lost (especially in infants).
4. Diabetes mellitus, in which some fatty acids react to produce ketone bodies, such as *acetoacetic acid, beta-hydroxybutyric acid,* and *acetone.* Normally these molecules are scarce and cells oxidize them as energy sources. However, if fats are used at an abnormally high rate, as may occur in diabetes mellitus, ketone bodies may accumulate faster than they can be oxidized and as a result spill over into the urine (ketonuria); in addition, the lungs may release acetone, which is volatile and imparts a fruity odor to the breath. More seriously, the accumulation of acetoacetic acid and beta-hydroxybutyric acid may lower pH (ketoacidosis). These acids may also combine with bicarbonate ions in the urine. Excess bicarbonate ions are excreted, interfering with the function of the bicarbonate acid-base buffer system.

Figure 18.12 summarizes the factors leading to metabolic acidosis. In each case, pH is lowered. Countering this lower pH are chemical buffer systems, which accept excess hydrogen ions; the respiratory center, which increases breathing rate and depth; and the kidneys, which excrete more hydrogen ions.

The symptoms of acidosis result from depression of central nervous system function. They include drowsiness, disorientation, stupor, and cyanosis. In uncompensated acidosis, the person may become comatose.

## Alkalosis

The two major types of alkalosis are *respiratory alkalosis* and *metabolic alkalosis.* Respiratory alkalosis results from excessive loss of carbon dioxide and consequent loss of carbonic acid. Metabolic alkalosis is due to excessive loss of hydrogen ions or gain of bases.

Respiratory alkalosis develops as a result of *hyperventilation* (described in chapter 16, p. 469), in which too much carbon dioxide is lost, decreasing carbonic acid and hydrogen ion concentrations. Hyperventilation may happen during periods of anxiety or may accompany fever or poisoning from salicylates, such as aspirin. At high altitudes, hyperventilation may be a response to low oxygen pressure. Musicians may hyperventilate to provide the large volume of air needed to play sustained passages on wind instruments. In each case, rapid, deep breathing depletes carbon dioxide, and the pH of body fluids increases. Figure 18.13 illustrates the factors leading to respiratory alkalosis.

Chemical buffers, such as hemoglobin, that release hydrogen ions resist the increase in pH. The lower levels of carbon dioxide and hydrogen ions stimulate the respiratory center to a lesser degree. This inhibits

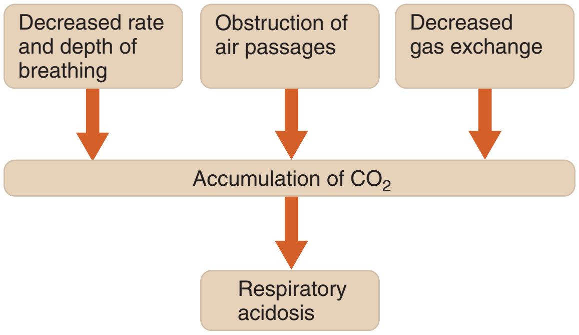

Decreased rate and depth of breathing
Obstruction of air passages
Decreased gas exchange
Accumulation of $CO_2$
Respiratory acidosis

**FIGURE 18.11** Some of the factors that lead to respiratory acidosis.

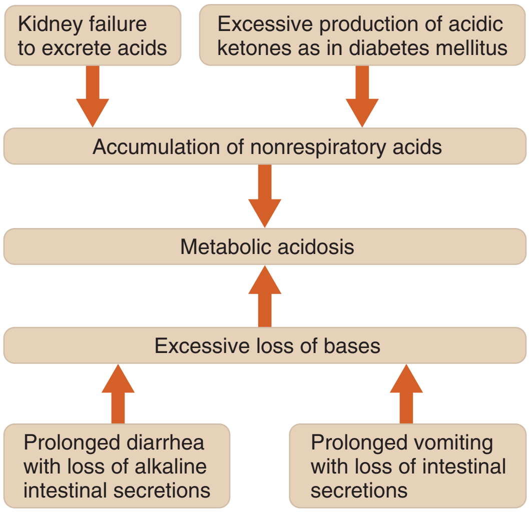

Kidney failure to excrete acids
Excessive production of acidic ketones as in diabetes mellitus
Accumulation of nonrespiratory acids
Metabolic acidosis
Excessive loss of bases
Prolonged diarrhea with loss of alkaline intestinal secretions
Prolonged vomiting with loss of intestinal secretions

**FIGURE 18.12** Some of the factors that lead to metabolic acidosis.

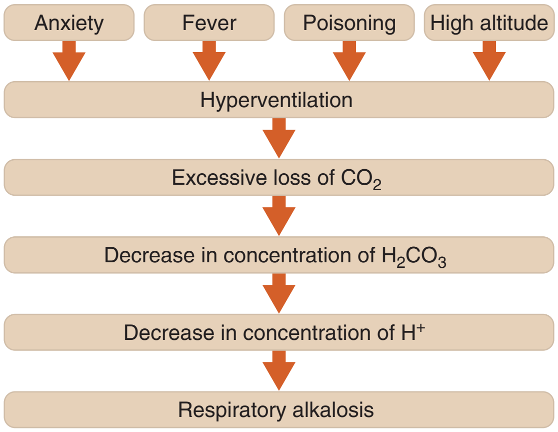

Anxiety
Fever
Poisoning
High altitude
Hyperventilation
Excessive loss of $CO_2$
Decrease in concentration of $H_2CO_3$
Decrease in concentration of $H^+$
Respiratory alkalosis

**FIGURE 18.13** Some of the factors that lead to respiratory alkalosis.

hyperventilation, thereby reducing further carbon dioxide loss. At the same time, the kidneys decrease their secretion of hydrogen ions, and the urine becomes alkaline as bases are excreted.

Metabolic alkalosis results from a loss of hydrogen ions or from a gain in bases, both accompanied by a rise in the pH of the blood (alkalemia). This condition may occur following gastric drainage (lavage), vomiting in which only the stomach contents are lost, or the use of certain diuretic drugs. Gastric juice is acidic, so its loss leaves body fluids more basic. Metabolic alkalosis may also develop as a result of ingesting too much antacid, such as sodium bicarbonate to relieve the symptoms of indigestion. Compensation for metabolic alkalosis includes a decrease in the breathing rate and depth, which in turn results in an increased concentration of carbon dioxide in the blood. Figure 18.14 illustrates the factors leading to metabolic alkalosis.

The symptoms of alkalosis include light-headedness, agitation, dizziness, and tingling sensations. In severe cases, impulses may be triggered spontaneously on motor neurons, and muscles may respond with tetanic contractions (see chapter 8, p. 199).

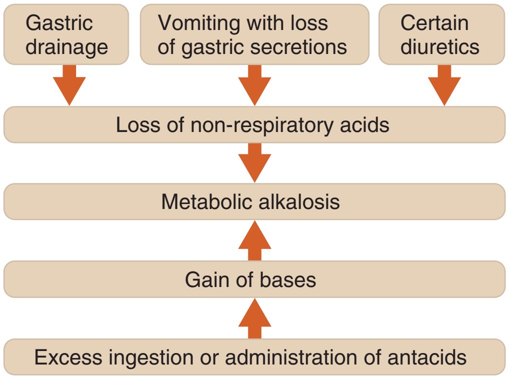

Gastric drainage
Vomiting with loss of gastric secretions
Certain diuretics
Loss of non-respiratory acids
Metabolic alkalosis
Gain of bases
Excess ingestion or administration of antacids

**FIGURE 18.14** Some of the factors that lead to metabolic alkalosis.

**PRACTICE**

26. What is the difference between a respiratory acid-base disturbance and a metabolic acid-base disturbance?
27. How do the symptoms of acidosis compare with those of alkalosis?

## Summary Outline

### 18.1 Introduction (p. 503)

*Maintenance of water and electrolyte balance requires that the quantities of these substances entering the body equal the quantities leaving it. Altering the water balance affects the electrolyte balance.*

### 18.2 Distribution of Body Fluids (p. 503)

1. Fluid compartments
   a. The intracellular fluid compartment includes the fluids and electrolytes cell membranes enclose.
   b. The extracellular fluid compartment includes all the fluids and electrolytes outside cell membranes.
2. Body fluid composition
   a. Extracellular fluids have high concentrations of sodium, chloride, calcium, and bicarbonate ions, with less potassium, magnesium, phosphate, and sulfate ions. Plasma contains more protein than does either interstitial fluid or lymph.
   b. Intracellular fluid contains high concentrations of potassium, magnesium, and phosphate ions. It also has a greater concentration of sulfate ions and lesser concentrations of sodium, chloride, calcium, and bicarbonate ions than does extracellular fluid.
3. Movement of fluid between compartments
   a. Hydrostatic and osmotic pressure regulate fluid movements.
   (1) Hydrostatic pressure forces fluid out of plasma, and colloid osmotic pressure returns fluid to plasma.
      (2) Hydrostatic pressure drives fluid into lymph vessels.
      (3) Osmotic pressure regulates fluid movement in and out of cells.
   b. Sodium ion concentrations are especially important in regulating fluid movement.

### 18.3 Water Balance (p. 505)

1. Water intake
   a. Most water comes from consuming liquids or moist foods.
   b. Oxidative metabolism produces some water.
   c. Thirst is the primary regulator of water intake.
   d. Drinking and the resulting stomach distension inhibit thirst.
2. Water output
   a. Water is lost in urine, feces, and sweat, and by evaporation from the skin and lungs.
   b. The distal convoluted tubules of the nephrons and the collecting ducts are the effectors of the control system that regulate water output.

### 18.4 Electrolyte Balance (p. 508)

1. Electrolyte intake
   a. The electrolytes of greatest importance to cellular functions in body fluids dissociate to release ions of sodium, potassium, calcium, magnesium, chloride, sulfate, phosphate, bicarbonate, and hydrogen.
   b. These ions are obtained in foods and beverages or as by-products of metabolic processes.
   c. Food and drink usually provide sufficient electrolytes.
   d. A severe electrolyte deficiency may produce a salt craving.
2. Electrolyte output
   a. Electrolytes are lost through perspiration, feces, and urine.
   b. Quantities lost vary with temperature and physical exercise.
   c. Most electrolytes are lost as a result of kidney function.
   d. Concentrations of sodium, potassium, and calcium ions in body fluids are particularly important.
   e. The adrenal cortex secretes aldosterone to regulate sodium and potassium ions.

   - f. Parathyroid hormone regulates calcium ions.
   - g. The mechanisms that control positively charged ions secondarily regulate negatively charged ions.

### 18.5 Acid-Base Balance (p. 509)

*Acids are electrolytes that release hydrogen ions. Bases release ions that combine with hydrogen ions. Body fluid pH must remain within a certain range.*

1. Sources of hydrogen ions
   - a. Aerobic respiration of glucose produces carbonic acid.
   - b. Anaerobic respiration of glucose produces lactic acid.
   - c. Incomplete oxidation of fatty acids releases acidic ketone bodies.
   - d. Oxidation of sulfur-containing amino acids produces sulfuric acid.
   - e. Hydrolysis of phosphoproteins and nucleic acids produces phosphoric acid.
2. Strengths of acids and bases
   - a. Acids vary in the extent to which they ionize to release ions.
     - (1) Strong acids, such as hydrochloric acid, ionize more completely.
     - (2) Weak acids, such as carbonic acid, ionize less completely.
   - b. Bases also vary in strength.
3. Regulation of hydrogen ion concentration
   - a. Chemical buffer systems
     - (1) Buffer systems convert strong acids into weaker acids or strong bases into weaker bases.
     - (2) They include the bicarbonate buffer system, phosphate buffer system, and protein buffer system.
     - (3) Buffer systems minimize pH changes.
   - b. The respiratory center controls the rate and depth of breathing to regulate pH.
   - c. The kidneys excrete hydrogen ions to regulate pH.
   - d. Chemical buffers act more rapidly. Physiological buffers act more slowly.

### 18.6 Acid-Base Imbalances (p. 512)

1. Acidosis
   - a. Respiratory acidosis results from increased levels of carbon dioxide and carbonic acid.
   - b. Metabolic acidosis results from accumulation of other acids or loss of bases.
2. Alkalosis
   - a. Respiratory alkalosis results from loss of carbon dioxide and carbonic acid.
   - b. Metabolic alkalosis results from loss of hydrogen ions or gain of bases.

## CHAPTER ASSESSMENTS

### 18.1 Introduction

**1.** Explain how water balance and electrolyte balance are interdependent. (p. 503)

### 18.2 Distribution of Body Fluids

**2.** Water and electrolytes enclosed by cell membranes constitute the ______________________. (p. 504)

a. transcellular fluid
b. intracellular fluid
c. extracellular fluid
d. lymph

**3.** Explain how the fluids in the compartments differ in composition. (p. 504)

**4.** Describe how fluid movements between the compartments are regulated. (p. 504)

### 18.3 Water Balance

**5.** Prepare a list of sources of normal water gain and loss to illustrate how the input of water equals the output of water. (pp. 505 and 508)

**6.** Define *water of metabolism.* (p. 505)

**7.** Explain how water intake is regulated. (p. 505)

**8.** Explain how the kidneys regulate water output. (p. 508)

### 18.4 Electrolyte Balance

**9.** Electrolytes in body fluids of importance to cellular functions include ______________________. (p. 508)

a. sodium
b. potassium
c. calcium
d. all of the above

**10.** Explain how electrolyte intake is regulated. (p. 508)

**11.** List the routes by which electrolytes leave the body. (p. 508)

**12.** Explain how the adrenal cortex functions to regulate electrolyte balance. (p. 509)

**13.** Describe the role of the parathyroid glands in regulating electrolyte balance. (p. 509)

### 18.5 Acid-Base Balance

**14.** List five sources of hydrogen ions in body fluids, and name an acid that originates from each source. (pp. 509–510)

**15.** ______________________ ionize more completely. An example is hydrochloric acid. (p. 510)

**16.** ______________________ dissociate to release fewer hydroxide ions. (p. 510)

**17.** Explain how the bicarbonate and phosphate buffer systems resist pH changes. (p. 511)

**18.** Explain why a protein has both acidic and basic properties. (p. 511)

**19.** Explain how the respiratory system and the kidneys function in the regulation of acid-base balance. (p. 512)

### 18.6 Acid-Base Imbalances

**20.** Distinguish between respiratory and metabolic acid-base imbalances. (pp. 513–515)

**21.** Explain how the body compensates for acid-base imbalances. (pp. 513–515)

## INTEGRATED ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 13.2, 13.4, 13.5, 14.3, 18.2

1. If the right ventricle of a patient's heart is failing, increasing the systemic venous pressure, what changes might occur in the patient's extracellular fluid compartments?

### OUTCOMES 15.2, 15.6, 15.9, 18.4, 18.6

2. Radiation therapy may damage the mucosa of the stomach and intestines. What effect might this have on the patient's electrolyte balance?

### OUTCOMES 15.9, 15.10, 17.2, 17.3, 18.5, 18.6

3. After eating an undercooked hamburger, a twenty-five-year-old male developed diarrhea due to infection with a strain of *Escherichia coli* that produces a shigatoxin. How would this affect his blood pH, urine pH, and respiratory rate?

### OUTCOMES 16.4, 16.5, 18.5, 18.6

4. A student hyperventilates and is disoriented just before an exam. Is this student likely to be experiencing acidosis or alkalosis? How will the body compensate in an effort to maintain homeostasis?

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# 19

# Reproductive Systems

Falsely colored, scanning electron micrograph of an egg being released from the surface of an ovary.

"Selling eggs." The ad in the student newspaper seemed too good to be true—the fee for donating a few eggs would pay nearly a semester's tuition. Intrigued, the young woman submitted a health history, had a checkup, and a month later received a call. A young couple struggling with infertility sought an egg donor. They'd chosen Sherrie because, with her strawberry-blond hair, she looked like Linda, the woman whose cancer had left her unable to conceive. The donor eggs would be fertilized in a laboratory dish (*in vitro*) with sperm from Linda's partner, and then implanted in Linda's uterus.

For two weeks Sherrie injected herself in the thigh with a drug that acts like gonadotropin-releasing hormone, suppressing release of an egg from an ovary (ovulation). When daily hormone checks indicated that her endocrine system was in sync with Linda's, Sherrie began giving herself shots twice a day at the back of the hip. This second drug mimicked follicle-stimulating hormone, and it caused several ovarian follicles, the structures that contain developing eggs, to mature. Finally, injections of luteinizing hormone brought the eggs close to being released. Then, at a health-care facility, Sherrie received pain medication and light sedation. A needle inserted through her vaginal wall retrieved a dozen mature eggs from the surface of her ovary.

Two *in vitro* fertilized ova divided a few times, forming pre-embryos that were implanted into Linda's uterus. The rest were frozen for possible later use. The preparation and procedure weren't too painful. Sherrie had felt a dull aching the last day before, and experienced bloating for a few days after the egg retrieval, but she did not experience bleeding, infection, cramping, or mood swings.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

**19.1 Introduction**

1. State the general functions of the male and female reproductive systems. (p. 519)

**19.2 Organs of the Male Reproductive System**

2. Describe the general function(s) of each part of the male reproductive system. (pp. 519–525)
3. Outline the process of spermatogenesis. (pp. 520–521)
4. Describe semen production and exit from the body. (pp. 521–525)

**19.3 Hormonal Control of Male Reproductive Functions**

5. Explain how hormones control the activities of the male reproductive organs and the development of male secondary sex characteristics. (pp. 526–528)

**19.4 Organs of the Female Reproductive System**

6. Describe the general function(s) of each part of the female reproductive system. (pp. 528–533)
7. Outline the process of oogenesis. (p. 529)

**19.5 Hormonal Control of Female Reproductive Functions**

8. Explain how hormones control the activities of the female reproductive organs and the development of female secondary sex characteristics. (pp. 534–535)
9. Describe the major events of a reproductive cycle. (pp. 535–536)

**19.6 Mammary Glands**

10. Review the structure of the mammary glands. (p. 538)

Anatomy & Physiology REVEALED aprevealed.com **Module 14** Reproductive System

**19.7 Birth Control**

**11.** Describe several methods of birth control, including the relative effectiveness of each method. (pp. 538–542)

**19.8 Sexually Transmitted Infections**

**12.** List the general symptoms of sexually transmitted infections. (p. 543)

## AIDS TO UNDERSTANDING WORDS *(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**andr-** [man] *andr*ogens: Male sex hormones.

**ejacul-** [to shoot forth] *ejacul*ation: Expulsion of semen from the male reproductive tract.

**fimb-** [fringe] *fimb*riae: Irregular extensions on the margin of the infundibulum of the uterine tube.

**follic-** [small bag] *follic*le: Ovarian structure that contains an egg.

**genesis-** [origin] spermato*genesis*: Formation of sperm cells.

**labi-** [lip] *labi*a minora: Flattened, longitudinal folds that extend along the margins of the female vestibule.

**mens-** [month] *mens*es: Monthly flow of blood from the female reproductive tract.

**mons-** [an eminence] *mons* pubis: Rounded elevation of fatty tissue overlying the pubic symphysis in a female.

**puber-** [adult] *puber*ty: The time in life when a person becomes able to reproduce.

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## 19.1 | Introduction

The male and female reproductive systems are each connected sets of organs and glands that produce and nurture sex cells (gametes) and transport them to sites of fertilization. Male sex cells are **sperm.** Female sex cells are eggs, or **oocytes** (o-o-sitz), which in Latin means "egg cells." Sex cells have one set of genetic instructions, carried on 23 chromosomes, compared to other, body cells, which have two sets on 46 chromosomes. When sex cells join at fertilization, the amount of genetic information held in 46 chromosomes is restored. Additionally, some of the reproductive organs secrete hormones vital to the development and maintenance of secondary sex characteristics and the regulation of reproductive functions.

### PRACTICE

1. What are the male and the female sex cells called?

## 19.2 | Organs of the Male Reproductive System

The *primary sex organs* (gonads) of the male reproductive system are the two testes, in which sperm cells and the male sex hormones are formed. The *accessory sex organs* (secondary sex organs) of the male reproductive system are the internal and external reproductive organs (fig. 19.1; reference plates 3 and 4, pp. 34–35).

### Testes

The **testes** (tes′tēz; sing., *testis*) are ovoid structures about 5 centimeters in length and 3 centimeters in diameter. Both testes are within the cavity of the saclike *scrotum.*

#### *Structure of the Testes*

A tough, white, fibrous capsule encloses each testis. Along the capsule's posterior border, the connective tissue thickens and extends into the testis, forming thin septa that subdivide the testis into about 250 *lobules.*

### CAREER CORNER
### Midwife

A couple chooses a certified nurse-midwife (CNM) to deliver their third child because they prefer a home birth. Their first two children had been delivered in a hospital, but they are healthy and the births were uncomplicated.

The nurse-midwife meets with the couple throughout the pregnancy, for at least an hour each time, and is present for the entire labor and birth. She uses soothing words and gentle massage to ease the baby into the world. The nurse-midwife places the newborn on the mother's chest while she completes the initial examination.

A CNM provides pregnancy care, but can also provide primary care, gynecologic care, family planning, treatment for sexually transmitted infections, and newborn care for the first month of life. He or she can do physical exams, prescribe medications, and order and interpret medical tests to provide a diagnosis.

A nurse-midwife is a registered nurse who has a graduate degree in midwifery from an accredited program, and has passed a certification or licensing exam. Many nurse-midwives deliver babies in patients' homes, but some are affiliated with hospitals. Nurse-midwives work with physicians who can help in case of emergency.

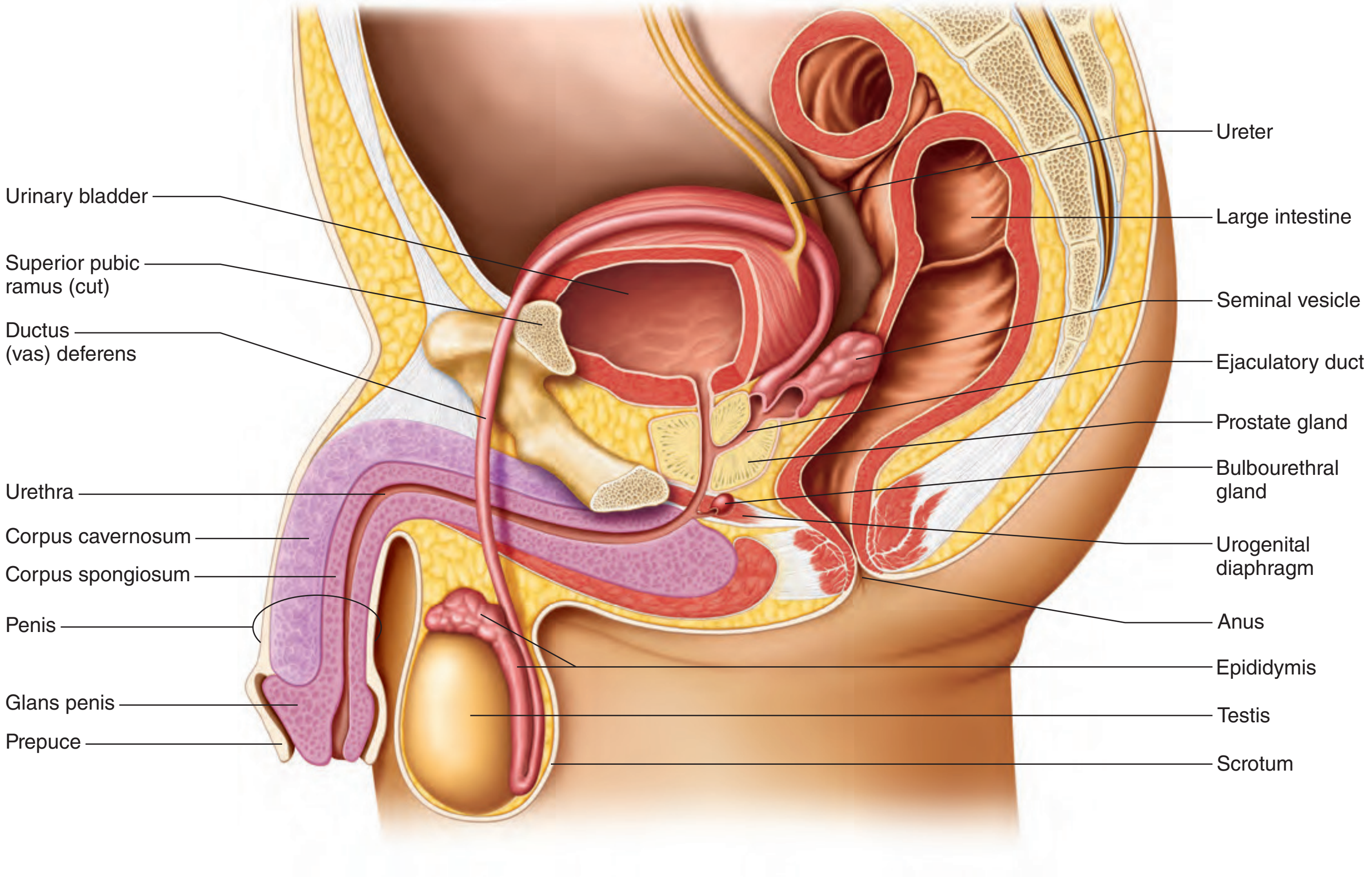

Urinary bladder
Superior pubic ramus (cut)
Ductus (vas) deferens
Urethra
Corpus cavernosum
Corpus spongiosum
Penis
Glans penis
Prepuce
Ureter
Large intestine
Seminal vesicle
Ejaculatory duct
Prostate gland
Bulbourethral gland
Urogenital diaphragm
Anus
Epididymis
Testis
Scrotum

**FIGURE 19.1** APR Male reproductive organs (sagittal view). The paired testes are the primary sex organs, and the other reproductive structures, both internal and external, are accessory sex organs.

A lobule contains one to four highly coiled, convoluted **seminiferous tubules** (se″mĭ-nif′er-us too′būlz), each approximately 70 centimeters long uncoiled. These tubules course posteriorly and unite to form a complex network of channels that give rise to several ducts that join a tube called the *epididymis.* The epididymis is coiled on the outer surface of the testis and continues to become the *ductus deferens* (fig. 19.2*a*).

A specialized stratified epithelium with **spermatogenic** (sper″mah-to-jen′ik) **cells** (germ cells), which give rise to sperm cells, lines the seminiferous tubules. Other specialized cells, called **interstitial cells** (cells of Leydig), lie in the spaces between the seminiferous tubules (fig. 19.2*b, c*). Interstitial cells produce and secrete male sex hormones.

The epithelial cells of the seminiferous tubules can give rise to *testicular cancer,* a common cancer in young men. In most cases the first sign is a painless testis enlargement or a scrotal mass attached to a testis. If a biopsy (tissue sample) reveals cancer cells, surgery is performed to remove the affected testis (orchiectomy). Radiation and/or chemotherapy often prevents the cancer from recurring.

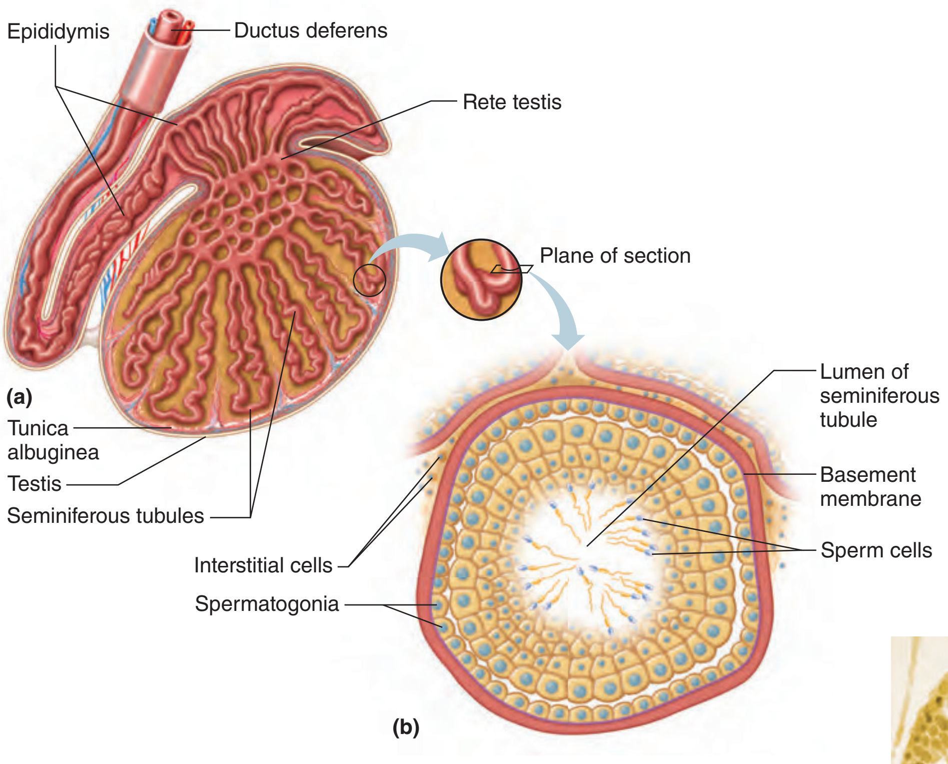
## PRACTICE

2. Describe the structure of a testis.
3. Where in the testes are the sperm cells produced?
4. Which cells produce male sex hormones?

### *Formation of Sperm Cells*

The epithelium of the seminiferous tubules consists of sustentacular cells (Sertoli cells) and spermatogenic cells. Sustentacular cells support, nourish, and regulate the spermatogenic cells.

In the male embryo, the undifferentiated spermatogenic cells are called **spermatogonia** (sper″mah-to-go′ne-ah). Each spermatogonium contains 46 chromosomes (23 pairs) in its nucleus, the usual number for human body cells. Beginning during embryonic development, hormones stimulate spermatogonia to undergo mitosis (see chapter 3, p. 80). Each cell division gives rise to two new cells, one of which (type A) maintains the supply of undifferentiated cells, the other of which (type B) differentiates, becoming a *primary spermatocyte.* Sperm cell production or **spermatogenesis** (sper″mah-to-jen′ĕ-sis) is arrested at this stage.


Epididymis
Ductus deferens
Rete testis
Plane of section
(a)
Tunica albuginea
Testis
Seminiferous tubules
Lumen of seminiferous tubule
Basement membrane
Sperm cells
Interstitial cells
Spermatogonia
(b)

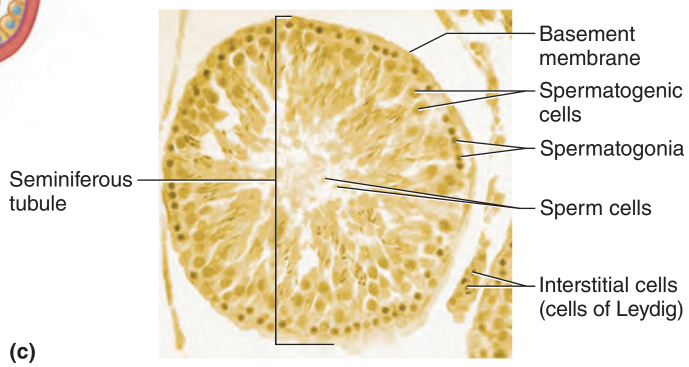

Basement membrane
Spermatogenic cells
Spermatogonia
Seminiferous tubule
Sperm cells
Interstitial cells (cells of Leydig)
(c)

**FIGURE 19.2** APR Structure of the testes. (**a**) Sagittal section of a testis. (**b**) Cross section of a seminiferous tubule. (**c**) Light micrograph of seminiferous tubules (250×).

At puberty mitosis resumes, and new spermatogonia form. Testosterone secretion increases and the primary spermatocytes then reproduce by a special type of cell division called **meiosis** (mi-o′sis) (fig. 19.3). Meiosis includes two successive divisions, called the *first* and *second meiotic divisions.* The first meiotic division (meiosis I) separates homologous chromosome pairs. Homologous pairs are the same, gene for gene. They may not be identical, however, because a gene may have variants, and the chromosome that comes from the person's mother may carry a different variant for the corresponding gene from the father's homologous chromosome. Before meiosis I, each homologous chromosome is replicated, so it consists of two complete DNA strands called *chromatids.* The chromatids of a replicated chromosome attach at regions called *centromeres.* Each chromatid has the complete genetic information associated with that chromosome.

Each of the cells that undergoes the second meiotic division (meiosis II) begins with one member of each homologous pair, a condition termed **haploid** (hap′loyd). That is, a haploid cell has one set of chromosomes. This second division separates the chromatids, producing cells that are still haploid, but whose chromosomes are no longer in the replicated form. After meiosis II, each of the chromatids is an independent chromosome (fig. 19.3). Consequently, for each primary spermatocyte that undergoes meiosis, four sperm cells, with 23 chromosomes in each of their nuclei, form. This is accomplished as each primary spermatocyte divides to form two *secondary spermatocytes.* Each of these cells, in turn, divides to form two *spermatids,* which mature into sperm cells (fig. 19.4).

Spermatogenesis occurs continually in a male, starting at puberty. The resulting sperm cells collect in the lumen of each seminiferous tubule, and then pass to the epididymis, where they accumulate and mature.

### *Structure of a Sperm Cell*

A mature sperm cell is a tiny, tadpole-shaped structure about 0.06 millimeters long. It consists of a flattened head, a cylindrical midpiece (body), and an elongated tail (fig. 19.5; see fig. 3.9*b*, p. 71).

The oval *head* of a sperm cell is primarily composed of a nucleus and contains highly compacted chromatin consisting of 23 chromosomes. A small protrusion at its anterior end, called the *acrosome,* contains enzymes that aid the sperm cell in penetrating the

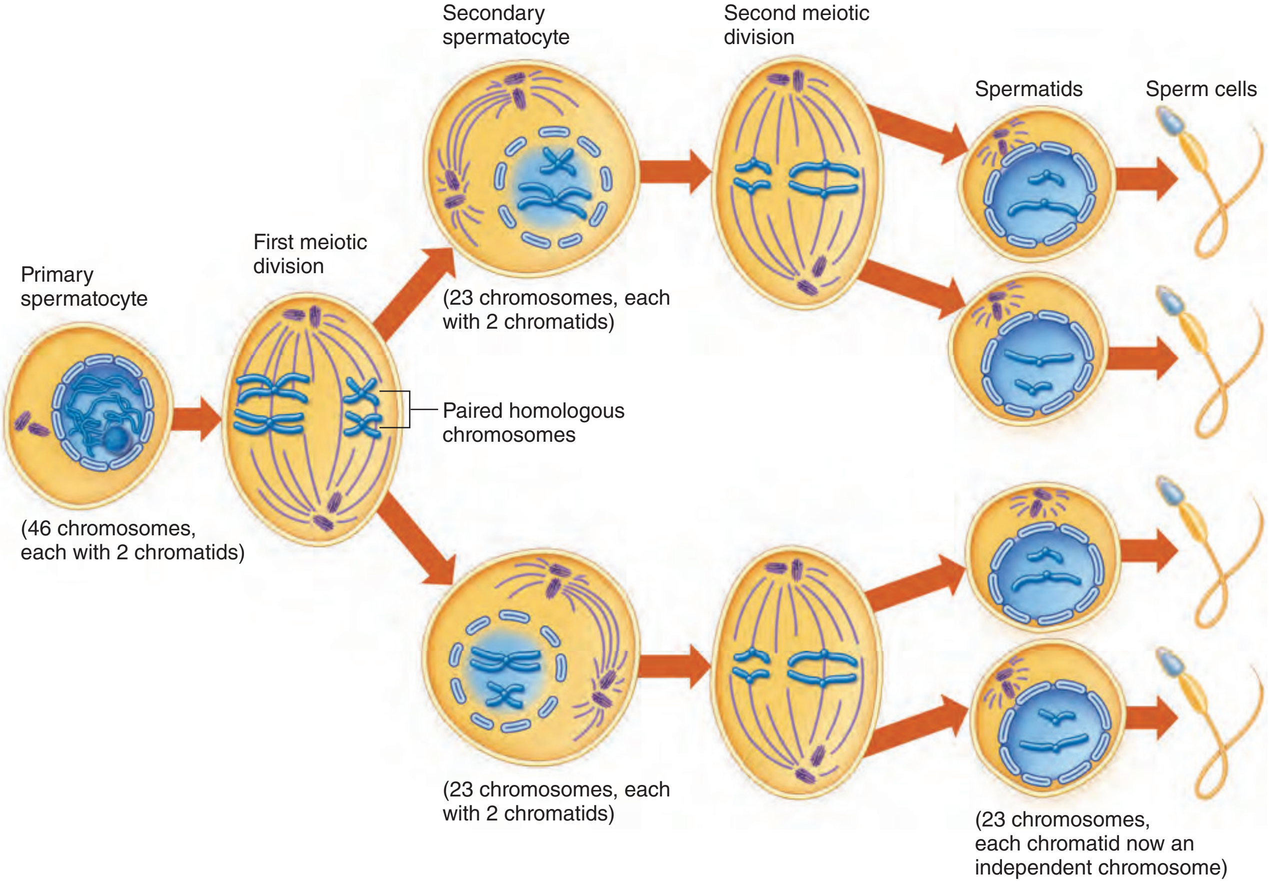

Secondary spermatocyte
Second meiotic division
Spermatids
Sperm cells
First meiotic division
Primary spermatocyte
(23 chromosomes, each with 2 chromatids)
Paired homologous chromosomes
(46 chromosomes, each with 2 chromatids)
(23 chromosomes, each with 2 chromatids)
(23 chromosomes, each chromatid now an independent chromosome)

**FIGURE 19.3** During spermatogenesis, there are two successive meiotic divisions.

**Q** *Why is it important that a sperm possess only 23 chromosomes?*
**Answer may be found in Appendix F on page 582.**

layers surrounding the oocyte during fertilization. An enzyme on the sperm cell membrane also contributes to this process. (Chapter 20, p. 552, describes this process.)

The *midpiece* of a sperm cell has a central, filamentous core and many mitochondria organized in a spiral. The *tail* (flagellum) consists of several microtubules enclosed in an extension of the cell membrane. The mitochondria provide ATP for the tail's lashing movement that propels the sperm cell through fluid.

**PRACTICE**

5. Explain the function of supporting cells in the seminiferous tubules.
6. Review the events of spermatogenesis.
7. Describe the structure of a sperm cell.

## Male Internal Reproductive Organs

The internal accessory organs of the male reproductive system are specialized to nurture and transport sperm cells. These structures include the two epididymides, two ductus deferentia, two ejaculatory ducts, and the urethra, as well as the two seminal vesicles, prostate gland, and two bulbourethral glands.

### *Epididymides*

The **epididymides** (ep″ĭ-di-dy′mides; sing., *epididymis*) are tightly coiled, threadlike tubes about 6 meters long (see figs. 19.1 and 19.2). Each epididymis is connected to ducts within a testis. It emerges from the top of the testis, descends along the posterior surface of the testis, and then courses upward to become the ductus deferens.

When sperm cells reach the epididymis, they are nonmotile. As rhythmic peristaltic contractions help move these cells through the epididymis, the cells mature. Following this aging process, the sperm cells can move independently and fertilize egg cells. However, they usually do not move independently until after ejaculation.

### *Ductus Deferentia*

The **ductus deferentia** (duk′tus def″er-en′sha; sing., *ductus deferens*), also called vasa deferentia, are muscular tubes about 45 centimeters long (see fig. 19.1). Each passes upward along the medial side of a testis and

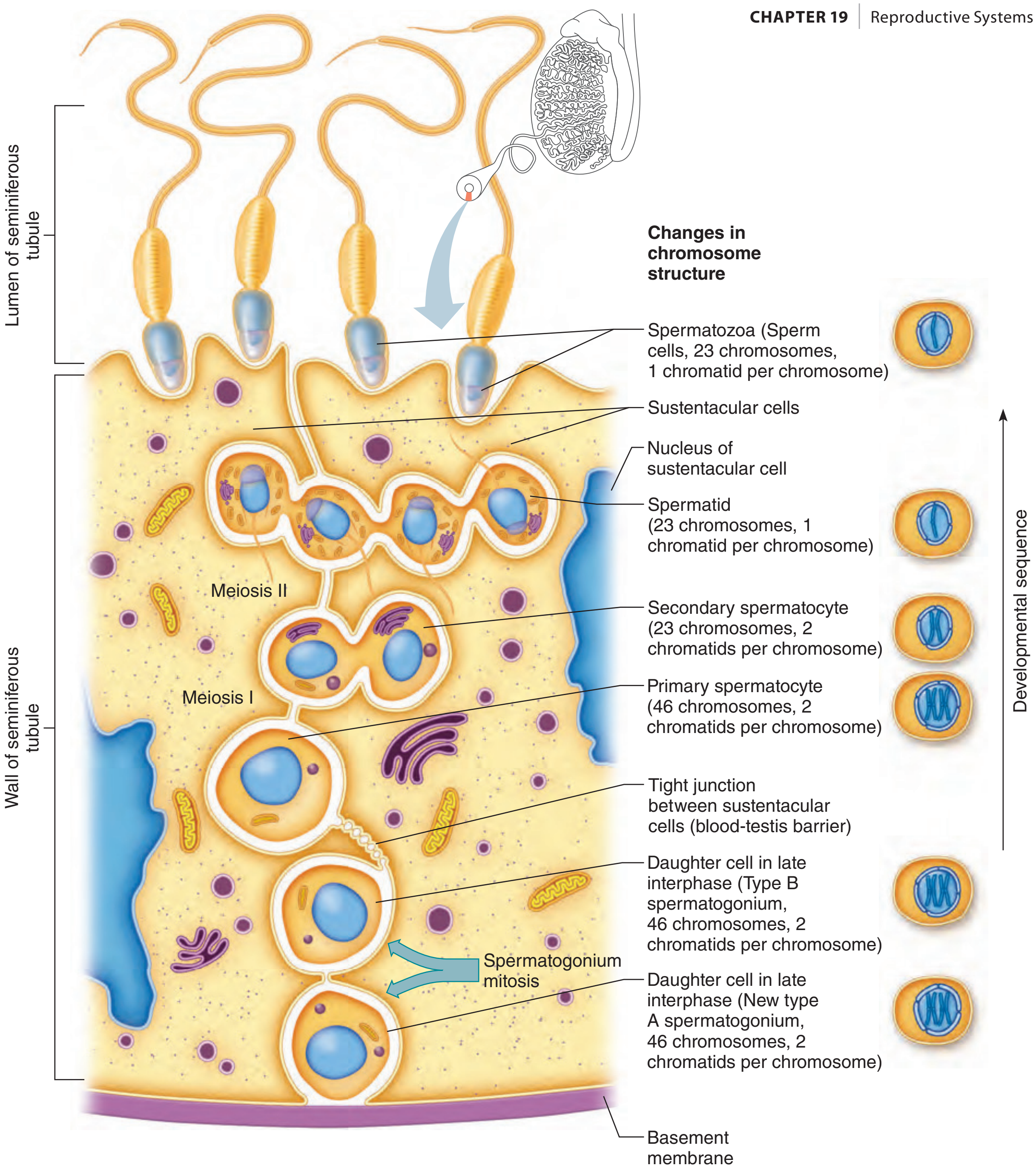

Lumen of seminiferous tubule
Wall of seminiferous tubule
Changes in chromosome structure
Spermatozoa (Sperm cells, 23 chromosomes, 1 chromatid per chromosome)
Sustentacular cells
Nucleus of sustentacular cell
Spermatid (23 chromosomes, 1 chromatid per chromosome)
Meiosis II
Secondary spermatocyte (23 chromosomes, 2 chromatids per chromosome)
Meiosis I
Primary spermatocyte (46 chromosomes, 2 chromatids per chromosome)
Tight junction between sustentacular cells (blood-testis barrier)
Daughter cell in late interphase (Type B spermatogonium, 46 chromosomes, 2 chromatids per chromosome)
Spermatogonium mitosis
Daughter cell in late interphase (New type A spermatogonium, 46 chromosomes, 2 chromatids per chromosome)
Basement membrane
Developmental sequence

**FIGURE 19.4** APR Mitosis in spermatogonia results in type A spermatogonia that continue the germ cell line and type B spermatogonia that give rise to primary spermatocytes. The primary spermatocytes, in turn, give rise to sperm cells by meiosis. Changes in chromosome number and structure are represented by a single pair of chromosomes. Note that as the cells approach the lumen they mature.

through a passage in the lower abdominal wall (inguinal canal), enters the pelvic cavity, and ends behind the urinary bladder. Just outside the prostate gland, the ductus deferens unites with the duct of a seminal vesicle to form an **ejaculatory duct,** which passes through the prostate gland and empties into the urethra.

### *Seminal Vesicles*

The **seminal vesicles** are convoluted, saclike structures about 5 centimeters long. Each attaches to the ductus deferens near the base of the urinary bladder (see fig. 19.1). The glandular tissue lining the inner wall of a seminal vesicle secretes a slightly alkaline fluid. This fluid helps regulate the pH of the tubular contents as sperm cells travel to the outside. Additionally, seminal fluid neutralizes the acidic secretions of the vagina, helping to sustain sperm cells that enter the female reproductive tract. Seminal vesicle secretions also contain *fructose,* a monosaccharide that provides energy to sperm cells, and *prostaglandins* (see chapter 11, p. 306), which stimulate muscular contractions within the female reproductive organs, aiding the movement of sperm cells toward the egg cell.

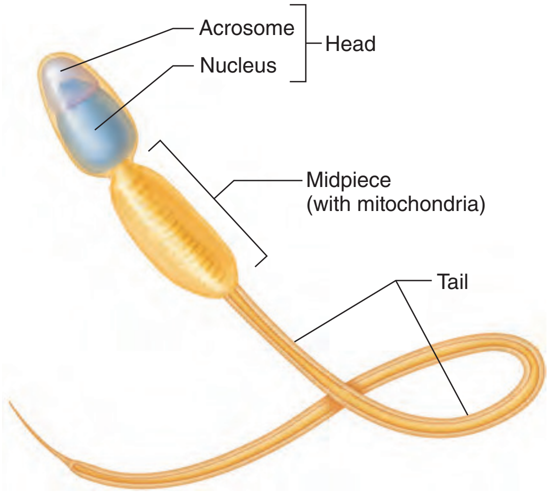


**FIGURE 19.5** Parts of a mature sperm cell.

### PRACTICE

8. Describe the structure of the epididymis.
9. Trace the path of the ductus deferens.
10. What is the function of a seminal vesicle?

### *Prostate Gland*

The **prostate** (pros′tāt) **gland** is a chestnut-shaped structure about 4 centimeters across and 3 centimeters thick that surrounds the proximal part of the urethra, just inferior to the urinary bladder (see fig. 19.1). It is enclosed in connective tissue and composed of many branched tubular glands whose ducts open into the urethra.

The prostate gland secretes a thin, milky fluid. This slightly acidic secretion also contains citrate, a nutrient for the sperm, and prostate-specific antigen (PSA), an enzyme which helps liquefy semen. Clinical Application 19.1 discusses prostate cancer.

The prostate gland is small in boys, begins to grow in early adolescence, and reaches adult size several years later. Usually the gland does not grow again until age fifty, when in about half of all men it enlarges enough to press on the urethra. The man feels the need to urinate frequently because the bladder cannot empty completely.

### *Bulbourethral Glands*

The two **bulbourethral** (bul″bo-u-re′thral) **glands** (Cowper's glands) are each about a centimeter in diameter and are inferior to the prostate gland (see fig. 19.1). Bulbourethral glands are composed of many tubes whose epithelial linings secrete a mucuslike fluid in response to sexual stimulation. This fluid lubricates the end of the penis in preparation for sexual intercourse. However, females secrete most of the lubricating fluid for sexual intercourse.

### *Semen*

**Semen** (se′men) is the fluid the male urethra conveys to the outside during ejaculation. It consists of sperm cells from the testes and secretions of the seminal vesicles, prostate gland, and bulbourethral glands. Semen is slightly alkaline (pH about 7.5), and it includes prostaglandins and nutrients.

The volume of semen released at one time varies from 2 to 5 milliliters. The average number of sperm cells in the fluid is about 120 million per milliliter.

Sperm cells remain nonmotile while in the ducts of the testis and epididymis, but begin to swim as they mix with accessory gland secretions. Sperm cells cannot fertilize an egg cell until they enter the female reproductive tract. Here, they undergo *capacitation,* which weakens the sperm cells' acrosomal membranes.

### PRACTICE

11. Where is the prostate gland located?
12. What is the function of the bulbourethral glands?
13. What are the components of semen?

## Male External Reproductive Organs

The male external reproductive organs are the scrotum, which encloses two testes, and the penis. The urethra passes through the penis.

### *Scrotum*

The **scrotum** is a pouch of skin and subcutaneous tissue that hangs from the lower abdominal region posterior to the penis (see fig. 19.1). A medial septum divides the scrotum into two chambers, each of which encloses a testis. Each chamber also contains a serous membrane, which covers the testis and helps it move smoothly within the scrotum. The scrotum protects and helps regulate the temperature of the testes. These factors are important to sex cell production.

Exposure to cold stimulates the smooth muscle fibers in the wall of the scrotum to contract, the scrotal skin to wrinkle, and the testes to move closer to the pelvic cavity, where they can absorb heat. Exposure to warmth stimulates the smooth muscle fibers to relax and the scrotum to hang loosely, providing an environment 3°C (about 5°F) below body temperature, which is more conducive to sperm production and survival.

### *Penis*

The **penis** is a cylindrical organ that conveys urine and semen through the urethra to the outside (see fig. 19.1). During erection, it enlarges and stiffens, enabling it to be inserted into the vagina during sexual intercourse.

## CLINICAL APPLICATION 19.1

### Prostate Cancer

Each year in the United States, nearly 200,000 men receive a diagnosis of prostate cancer, and about 25,000 die of the disease. The diagnostic process typically begins with a rectal exam in which a health care practitioner feels an enlargement of the prostate gland, and a blood test to detect elevated levels of a biomarker called prostate-specific antigen (PSA). Normally, secretory epithelium in the prostate gland releases PSA, which liquefies the ejaculate. When cancer cells accumulate, more PSA is produced, and it enters capillaries in the prostate. If the elevated PSA is still present on a test a few months later, the next step is a biopsy procedure to sample cells from several sites in the gland. If cancer is detected, it is assigned a two-digit number, called a Gleason score, which indicates how specialized the cancer cells are. The less specialized the cancer cells, the more aggressive the disease. Imaging technologies can be used to assess whether the cancer has spread beyond the prostate capsule. In addition, researchers are identifying other protein biomarkers (see Clinical Application 2.2, page 57) in which changing levels indicate a spreading cancer.

Treatment of prostate cancer may be necessary if the tumor has a high Gleason score or has biomarkers indicating likelihood of spread. Treatments include surgery to remove the prostate gland, radiation, and hormones. Adverse effects of treatment include urinary incontinence and erectile dysfunction, which may improve with time. For many men active surveillance to regularly monitor the disease is sufficient. This means PSA tests twice a year and a biopsy every one to two years, with treatment if the condition worsens.

The *body,* or shaft, of the penis has three columns of erectile tissue—a pair of dorsally located *corpora cavernosa* and a single, ventral *corpus spongiosum.* A tough capsule of dense connective tissue surrounds each column. Skin, a thin layer of subcutaneous tissue, and a layer of connective tissue enclose the penis.

The corpus spongiosum, through which the urethra extends, enlarges at its distal end to form a sensitive, cone-shaped **glans penis.** The glans covers the ends of the corpora cavernosa and bears the urethral opening (external urethral orifice). The skin of the glans is very thin and hairless, and contains sensory receptors for sexual stimulation. A loose fold of skin called the *prepuce* (foreskin) originates just posterior to the glans and extends anteriorly to cover it as a sheath. A surgical procedure called *circumcision* removes the prepuce.

**PRACTICE**

14. Describe the structure of the penis.
15. What is circumcision?

## Erection, Orgasm, and Ejaculation

During sexual stimulation, parasympathetic impulses from the sacral part of the spinal cord release nitric oxide (NO), which dilates the arteries leading into the penis, increasing blood flow into erectile tissues. At the same time, the increasing pressure of arterial blood entering the vascular spaces of erectile tissue compresses the veins of the penis, reducing the flow of venous blood away from the organ. Consequently, blood accumulates in the erectile tissues, and the penis swells and elongates, producing an **erection.**

The culmination of sexual stimulation is **orgasm** (or′gazm), a pleasurable feeling of physiological and psychological release. Orgasm in the male is accompanied by emission and ejaculation.

**Emission** (e-mish′un) is the movement of sperm cells from the testes and secretions from the prostate gland and seminal vesicles into the urethra, where they mix to form semen. Emission is a response to sympathetic impulses from the spinal cord, which stimulate peristaltic contractions in smooth muscle in the walls of the testicular ducts, epididymides, ductus deferentia, and ejaculatory ducts. Other sympathetic impulses stimulate rhythmic contractions of the seminal vesicles and prostate gland.

As the urethra fills with semen, sensory impulses pass into the sacral part of the spinal cord. In response, motor impulses are conducted from the spinal cord to certain skeletal muscles at the base of the penile erectile columns, rhythmically contracting them. This increases the pressure in the erectile tissues and aids in forcing the semen through the urethra to the outside, a process called **ejaculation** (e-jak″u-la′shun). At the time of ejaculation, the posterior pituitary gland releases a burst of oxytocin, which stimulates contractions of the epididymides, seminiferous tubules, and prostate gland, aiding the movement of sperm.

The sequence of events during emission and ejaculation is coordinated so that the fluid from the bulbourethral glands is expelled first. This is followed by the release of fluid from the prostate gland, the passage of sperm cells, and finally the ejection of fluid from the seminal vesicles.

Immediately after ejaculation, sympathetic impulses constrict the arteries that supply the erectile tissue, reducing inflow of blood. Smooth muscle in the walls of the vascular spaces partially contracts, and the veins of the penis carry excess blood out of these spaces. The penis gradually returns to its flaccid state. Table 19.1 summarizes the functions of the male reproductive organs. Clinical Application 19.2 discusses male infertility.

Spontaneous emission and ejaculation are common in sleeping adolescent males. Changes in hormonal concentrations that accompany adolescent development and sexual maturation cause these events.

### PRACTICE

16. What controls blood flow into penile erectile tissues?
17. Distinguish among orgasm, emission, and ejaculation.
18. Review the events associated with emission and ejaculation.

**TABLE 19.1** Functions of the Male Reproductive Organs

| Organ | Function |
|---|---|
| Testis | |
| Seminiferous tubules | Produce sperm cells |
| Interstitial cells | Produce and secrete male sex hormones |
| Epididymis | Promotes sperm cell maturation; stores sperm cells; conveys sperm cells to ductus deferens |
| Ductus deferens | Conveys sperm cells to ejaculatory duct |
| Seminal vesicle | Secretes an alkaline fluid containing nutrients and prostaglandins that helps regulate pH of semen |
| Prostate gland | Secretes a slightly acidic fluid that contains citrate, a nutrient for sperm |
| Bulbourethral gland | Secretes fluid that lubricates end of penis |
| Scrotum | Encloses, protects, and regulates temperature of testes |
| Penis | Conveys urine and semen to outside of body; inserted into vagina during sexual intercourse; the glans penis is richly supplied with sensory nerve endings associated with feelings of pleasure during sexual stimulation |

## 19.3 Hormonal Control of Male Reproductive Functions

The hypothalamus, anterior pituitary gland, and testes secrete hormones that control male reproductive functions. These hormones initiate and maintain sperm cell production and oversee the development and maintenance of male secondary sex characteristics.

### Hypothalamic and Pituitary Hormones

The male body before ten years of age is reproductively immature with undifferentiated spermatogenic cells. Then, a series of changes leads to development of a reproductively functional adult. The hypothalamus controls many of these changes.

Recall from chapter 11 (p. 307) that the hypothalamus secretes gonadotropin-releasing hormone (GnRH), which enters the blood vessels leading to the anterior pituitary gland. In response, the anterior pituitary secretes the **gonadotropins** (go-nad″o-trōp′inz) *luteinizing hormone (LH)* and *follicle-stimulating hormone (FSH)*. LH, which in males has been referred to as interstitial cell stimulating hormone (ICSH), promotes development of interstitial cells of the testes, and they, in turn, secrete male sex hormones. FSH stimulates the sustentacular cells of the seminiferous tubules to respond to the effects of the male sex hormone *testosterone*. Then, in the presence of FSH and testosterone, these cells stimulate spermatogenic cells to undergo spermatogenesis, giving rise to sperm cells (fig. 19.6). The sustentacular cells also secrete a hormone called *inhibin,* which inhibits the anterior pituitary gland by negative feedback. This action prevents oversecretion of FSH.

### Male Sex Hormones

Male sex hormones are termed **androgens** (an′dro-jenz). Interstitial cells of the testes produce most of them, but small amounts are synthesized in the adrenal cortex (see chapter 11, p. 316). **Testosterone** (tes-tos′tĕ-rōn) is the most important androgen. It is secreted by the testes and transported in the blood, loosely attached to plasma proteins.

Testosterone secretion begins during fetal development and continues for several weeks following birth; then it nearly ceases during childhood. Between the ages of thirteen and fifteen, a young man's androgen production usually increases rapidly. This phase in development, when an individual becomes reproductively functional, is **puberty** (pu′ber-te). After puberty, testosterone secretion continues throughout the life of a male.

#### *Actions of Testosterone*

During puberty, testosterone stimulates enlargement of the testes and accessory organs of the reproductive system, as well as development of *male secondary sex*

## CLINICAL APPLICATION 19.2

## Male Infertility

Male infertility has several causes. If, during fetal development, the testes do not descend into the scrotum, the higher temperature of the abdominal cavity or inguinal canal hinders development of sperm cells in the seminiferous tubules. Certain diseases, such as mumps, may inflame the testes (orchitis), impairing fertility.

The quality and the quantity of sperm cells are essential factors in the ability of a man to father a child. If a sperm head is misshapen, if a sperm cell cannot swim, or if too few sperm cells reach the well-protected egg cell, fertilization may not happen.

Computer-aided semen analysis (CASA) is a technique used to evaluate a man's fertility. For this analysis, a man abstains from intercourse for two to three days and then provides a sperm sample. The man also provides information about his reproductive history and possible exposure to toxins. The CASA system captures images with a digital camera and analyzes and integrates information on sperm cell density, motility, and morphology. The result is a "spermiogram." Figure 19A shows a CASA of normal sperm cells, depicting different swimming patterns as they travel. Table 19A lists the components of a semen analysis.

**TABLE 19A Semen Analysis**

| Characteristic | Sperm Cell Density (million cells/milliliter) | Sperm Motility | Normal Sperm Morphology |
|---|---|---|---|
| Fertile | >40 | >50% | >30% |
| Borderline fertile | 20–40 | >50% | >14–30% |
| Infertile | <20 | <50% | <14% |

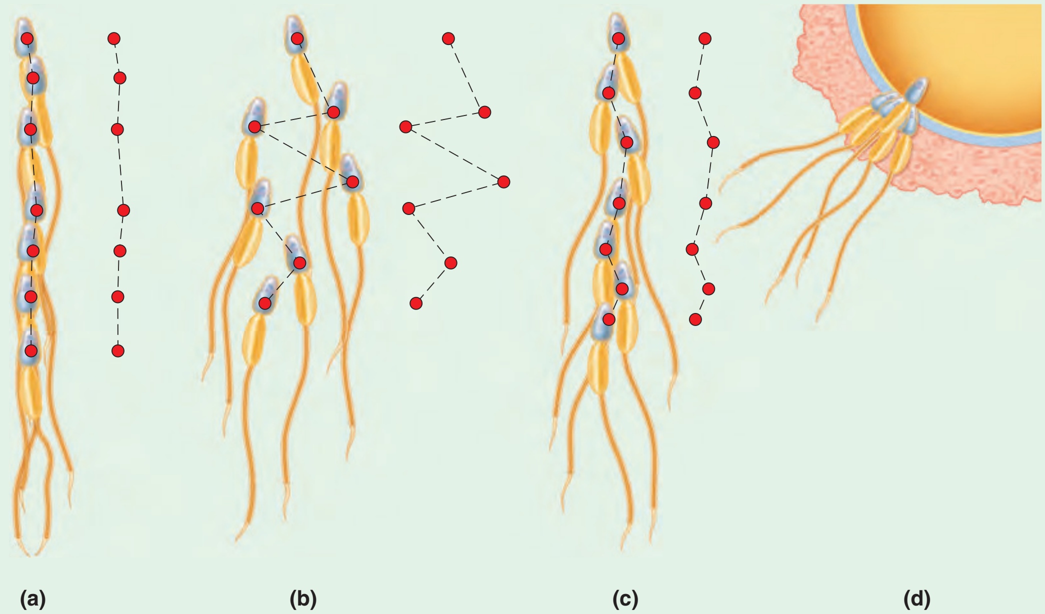


**FIGURE 19A** A computer tracks sperm cell movements. In semen, sperm cells swim in a straight line (**a**), but as they are activated by biochemicals in the woman's body, their trajectories widen (**b**). The sperm cells in (**c**) are in the mucus of a woman's cervix, and the sperm cells in (**d**) are attempting to digest through the structures surrounding an egg cell.

*characteristics,* which are special features associated with the adult male body. Secondary sex characteristics in the male include:

1. increased growth of body hair, particularly on the face, chest, axillary region, and pubic region. Sometimes, hair growth on the scalp slows.
2. enlargement of the larynx and thickening of the vocal folds, with lowering of the pitch of the voice.
3. thickening of the skin.
4. increased muscular growth, broadening of the shoulders, and narrowing of the waist.
5. thickening and strengthening of the bones.

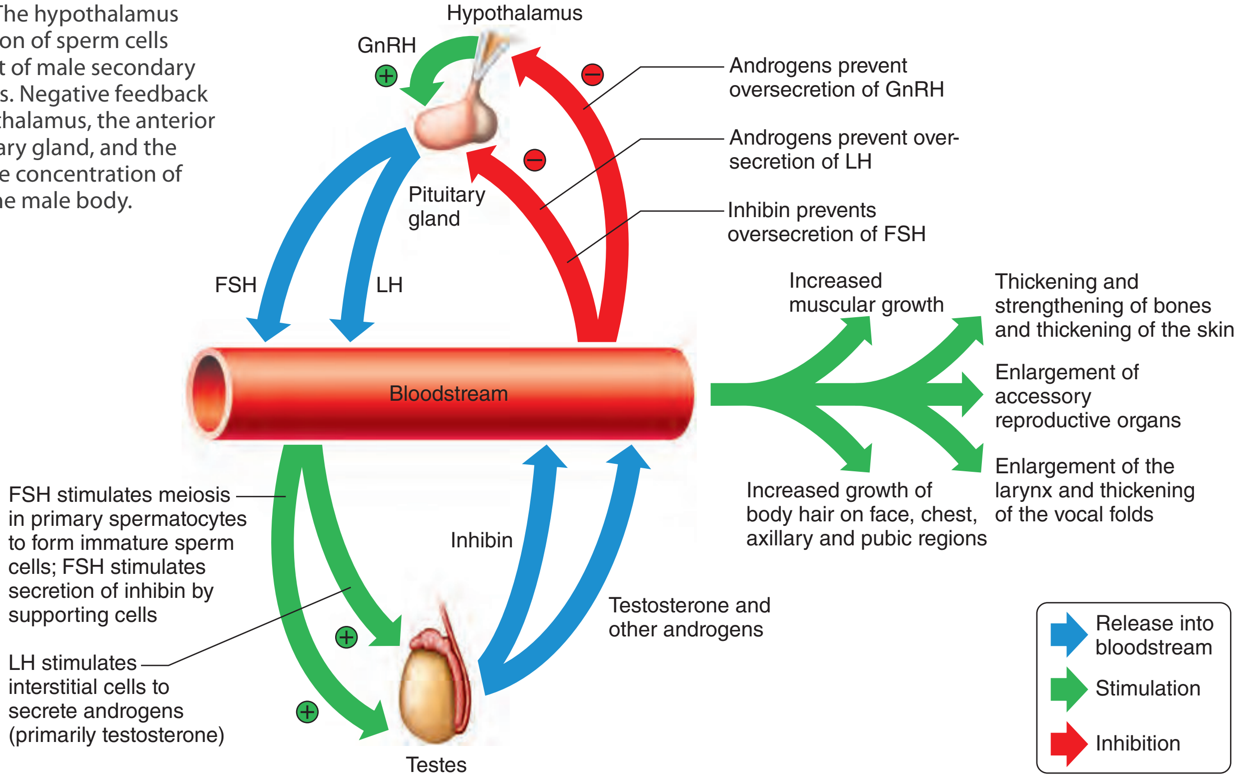

Hypothalamus
GnRH
Pituitary gland
FSH
LH
Androgens prevent oversecretion of GnRH
Androgens prevent oversecretion of LH
Inhibin prevents oversecretion of FSH
Bloodstream
Increased muscular growth
Thickening and strengthening of bones and thickening of the skin
Enlargement of accessory reproductive organs
Enlargement of the larynx and thickening of the vocal folds
Increased growth of body hair on face, chest, axillary and pubic regions
FSH stimulates meiosis in primary spermatocytes to form immature sperm cells; FSH stimulates secretion of inhibin by supporting cells
LH stimulates interstitial cells to secrete androgens (primarily testosterone)
Inhibin
Testosterone and other androgens
Testes
Release into bloodstream
Stimulation
Inhibition

**FIGURE 19.6** The hypothalamus controls maturation of sperm cells and development of male secondary sex characteristics. Negative feedback among the hypothalamus, the anterior lobe of the pituitary gland, and the testes controls the concentration of testosterone in the male body.

Testosterone also increases the rate of cellular metabolism and red blood cell production. For this reason, the average number of red blood cells in a microliter of blood is usually greater in males than in females. Testosterone stimulates sexual activity by affecting certain parts of the brain.

### *Regulation of Male Sex Hormones*

The extent to which male secondary sex characteristics develop is directly related to the amount of testosterone that interstitial cells secrete. The hypothalamus regulates testosterone output through negative feedback (fig. 19.6).

An increasing blood testosterone concentration inhibits the hypothalamus, and hypothalamic stimulation of the anterior pituitary gland by GnRH decreases. As the pituitary gland's secretion of LH falls in response, testosterone release from the interstitial cells decreases.

As the blood testosterone concentration drops, the hypothalamus becomes less inhibited, and it once again stimulates the anterior pituitary gland to release LH. Increasing LH secretion then causes interstitial cells to release more testosterone, and the blood testosterone concentration increases.

Testosterone level decreases somewhat during and after the *male climacteric,* which is a decline in sexual function associated with aging. At any given age, the testosterone concentration in the male body is regulated to remain relatively constant.

**PRACTICE**

19. Which hormone initiates the changes associated with male sexual maturity?
20. Describe several male secondary sex characteristics.
21. List the functions of testosterone.
22. Explain how the secretion of male sex hormones is regulated.

## 19.4 | Organs of the Female Reproductive System

The organs of the female reproductive system produce and maintain the female sex cells, the egg cells (or oocytes); transport these cells to the site of fertilization; provide a favorable environment for a developing offspring; move the offspring to the outside; and produce female sex hormones. The *primary sex organs* (gonads) of this system are the two ovaries, which produce the female sex cells and sex hormones. The *accessory sex organs* (secondary sex organs) of the female reproductive system are the internal and external reproductive organs (fig. 19.7; reference plates 5 and 6, pp. 36–37).

### Ovaries

The two **ovaries** are solid, ovoid structures, each about 3.5 centimeters long, 2 centimeters wide, and 1 centimeter thick. The ovaries lie in shallow depressions in the lateral wall of the pelvic cavity (fig. 19.7).

### Ovary Structure

Ovarian tissues are divided into two indistinct regions—an inner *medulla* and an outer *cortex*. The ovarian medulla is mostly composed of loose connective tissue and contains many blood vessels, lymphatic vessels, and nerve fibers. The ovarian cortex consists of more compact tissue and has a granular appearance due to tiny masses of cells called *ovarian follicles*.

A layer of cuboidal epithelium covers the ovary's free surface. Just beneath this epithelium is a layer of dense connective tissue.

## PRACTICE

23. What are the primary sex organs of the female?
24. Describe the structure of an ovary.

### Primordial Follicles

During prenatal (before birth) development of a female, small groups of cells in the outer region of the ovarian cortex form several million **primordial follicles.** Each follicle is a single, large cell, called a *primary oocyte*, surrounded by epithelial cells called *follicular cells*.

Early in development, the primary oocytes begin to undergo meiosis, but the process soon halts and does not continue until the individual reaches puberty. Once the primordial follicles appear, no new ones form. Instead, the number of oocytes in the ovary steadily declines as many of the oocytes degenerate. Of the several million oocytes that formed in the embryo, only a million or so remain at birth, and perhaps 400,000 are present at puberty. Of these, probably fewer than 400 or 500 oocytes will be released from the ovary during a female's reproductive life.

### Oogenesis

**Oogenesis** (o″o-jen′ĕ-sis) is the process of egg cell formation. Beginning at puberty, some primary oocytes are stimulated to continue meiosis. Like sperm cells, the resulting cells have one-half as many chromosomes (23) in their nuclei as their parent cells.

Unlike a primary spermatocyte, when a primary oocyte divides, the cytoplasm is distributed unequally. One of the resulting cells, called a *secondary oocyte* (egg cell), is large, and the other, called the *first polar body*, is small (fig. 19.8). The large secondary oocyte represents a future *egg cell* (ovum) that can be fertilized by uniting with a sperm cell. If this happens, the secondary oocyte divides unequally to produce a tiny *second polar body* and a large fertilized egg cell, also called a **zygote** (zi′gōt).

The polar bodies have no further function and soon degenerate. Their role in reproduction allows for pro-

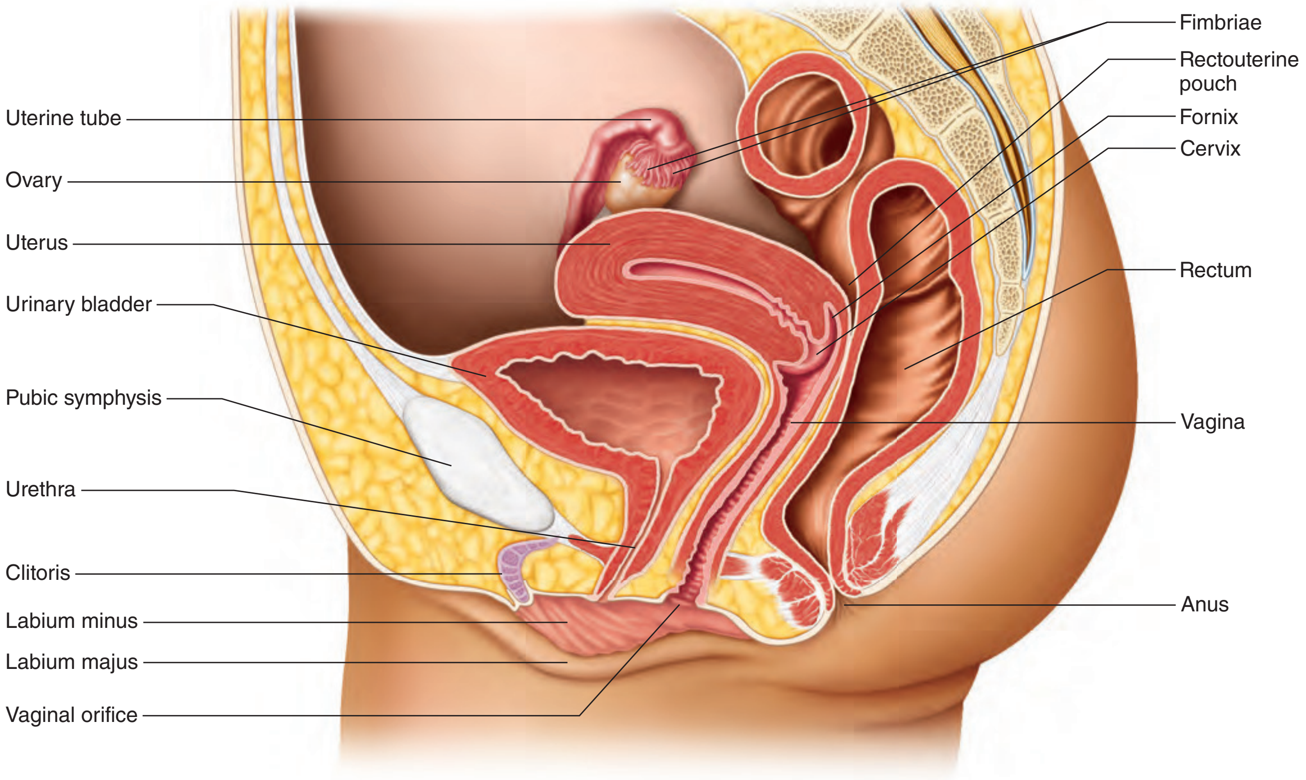


**FIGURE 19.7** APR Female reproductive organs (sagittal view). The paired ovaries are the primary sex organs, and the other reproductive structures, both internal and external, are accessory sex organs.

duction of an egg cell that has the massive amounts of cytoplasm and the abundant organelles required to carry the zygote through the first few cell divisions.

**FACTS OF LIFE** The largest cell in the human body is the egg. The smallest cell is the sperm.

## PRACTICE

25. Describe the major events of oogenesis.
26. What is the function of polar body formation?

### *Follicle Maturation*

At puberty, the anterior pituitary gland secretes increased amounts of FSH, and the ovaries enlarge in response. Throughout a woman's reproductive years, primordial follicles mature into **primary follicles** (pri′ma-re fol′ĭ-klz). Figure 19.9 traces the maturation of a follicle in an ovary.

During early follicle maturation, the primary oocyte within the follicle enlarges, and surrounding follicular cells proliferate by mitosis. These follicular cells organize into layers, and eventually a cavity (*antrum*) appears in the cellular mass and the structure is now called an **antral follicle**. A clear *follicular fluid* fills the antrum (fig. 19.9).

In time, the antral follicle reaches a diameter of 10 millimeters or more and bulges outward on the ovary surface. The oocyte within the mature antral follicle is a large, spherical cell, surrounded by a layer of glycoprotein called the zona pellucida and attached to a mantle of follicular cells (corona radiata) (fig. 19.10). Processes from these follicular cells extend through the zona pellucida and supply nutrients to the oocyte.

Although as many as twenty primary follicles may begin maturing at any one time, one follicle usually outgrows the others. Typically, only the dominant follicle fully develops, and the other follicles degenerate. This entire process, from a primordial follicle to a dominant, fully developed antral follicle, takes almost 300 days. The process is ongoing in the ovaries, such that a new dominant antral follicle becomes ready for ovulation approximately every 28 days.

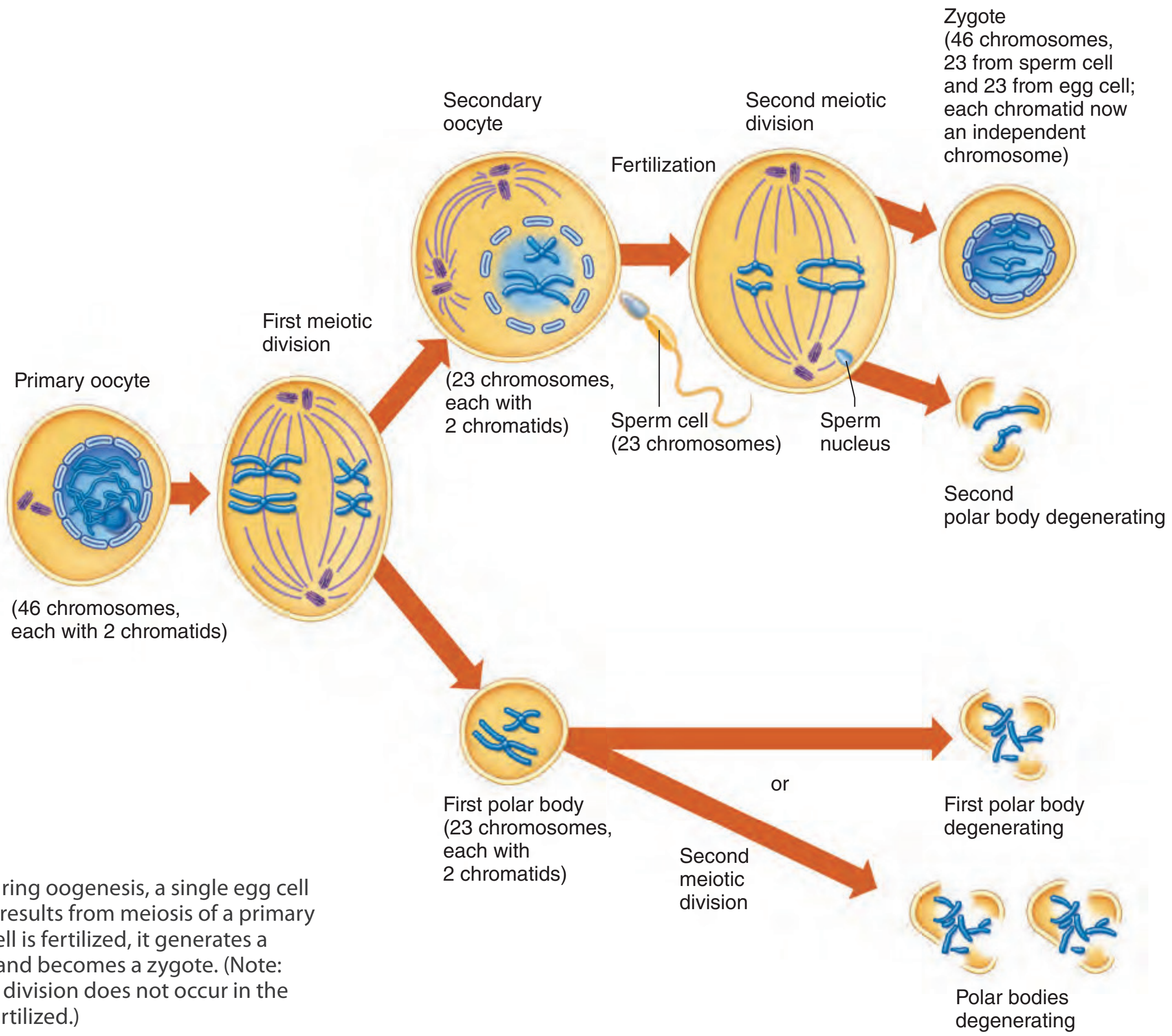

Zygote (46 chromosomes, 23 from sperm cell and 23 from egg cell; each chromatid now an independent chromosome)
Secondary oocyte
Second meiotic division
Fertilization
First meiotic division
Primary oocyte
(23 chromosomes, each with 2 chromatids)
Sperm cell (23 chromosomes)
Sperm nucleus
Second polar body degenerating
(46 chromosomes, each with 2 chromatids)
or
First polar body (23 chromosomes, each with 2 chromatids)
First polar body degenerating
Second meiotic division
Polar bodies degenerating

**FIGURE 19.8** During oogenesis, a single egg cell (secondary oocyte) results from meiosis of a primary oocyte. If the egg cell is fertilized, it generates a second polar body and becomes a zygote. (Note: The second meiotic division does not occur in the egg cell if it is not fertilized.)

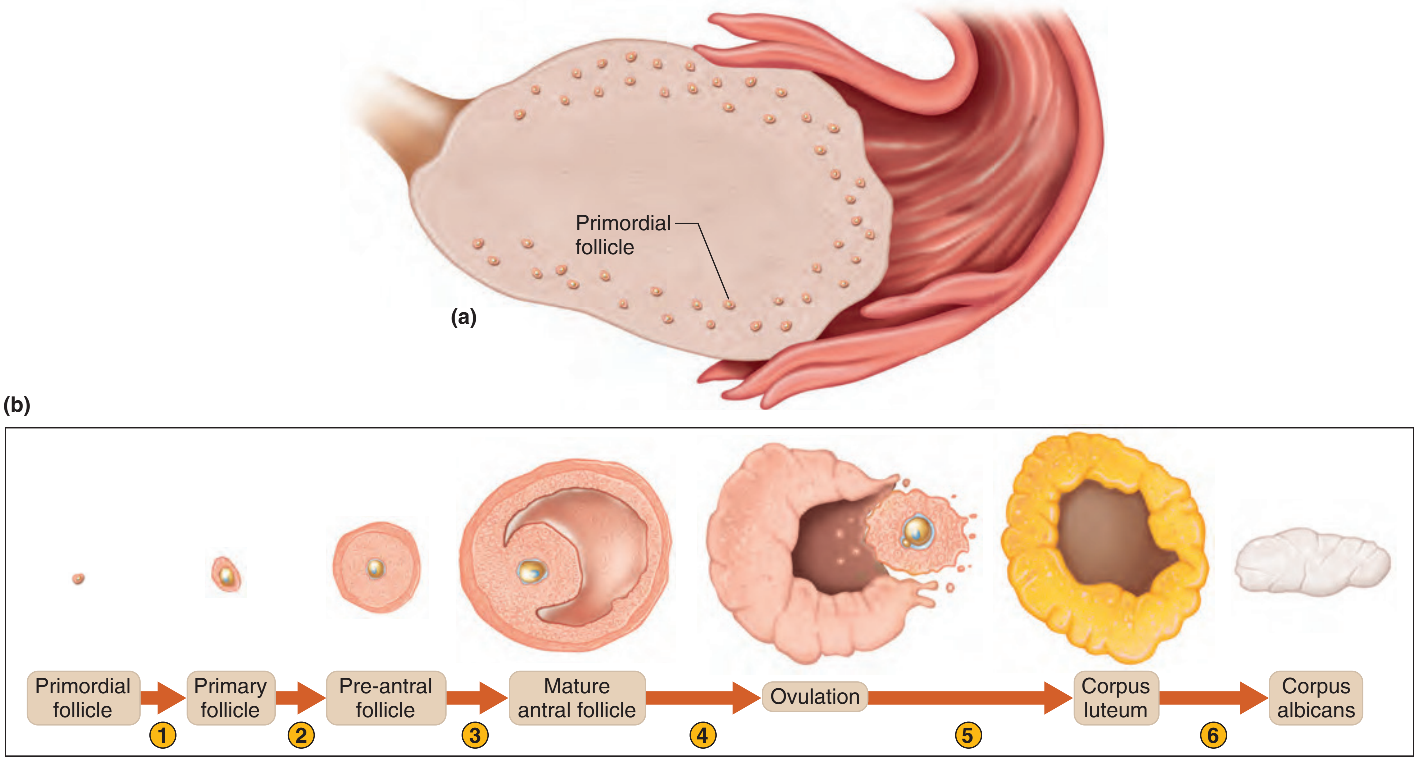


**FIGURE 19.9** APR Primordial follicles (**a**) in an ovary. (**b**) Follicular changes. (**1**), (**2**), (**3**) a developing primary oocyte enlarges and becomes surrounded by follicular cells and fluid. Eventually, (**4**) the mature follicle ruptures, releasing the secondary oocyte and layers of surrounding follicular cells. (**5**) The remainder of the mature follicle becomes the hormone-secreting corpus luteum. (**6**) If fertilization does not occur, the corpus luteum degenerates into the corpus albicans.

### *Ovulation*

Just prior to ovulation, a primary oocyte completes meiosis I, giving rise to a secondary oocyte and a first polar body. A process called **ovulation** (o″vu-la′shun) releases these cells from the mature antral follicle.

Release of LH from the anterior pituitary gland plays a role in triggering ovulation, during which the mature antral follicle swells and its wall weakens. Eventually, the wall ruptures, and follicular fluid, accompanied by the secondary oocyte, is released from the ovary's surface (see fig. 19.9).

After ovulation, the secondary oocyte and one or two layers of follicular cells surrounding it are normally propelled to the opening of a nearby uterine tube (fig. 19.11). If the secondary oocyte is not fertilized within hours, it degenerates.

### PRACTICE

27. Describe changes that occur in a follicle and its oocyte during maturation.
28. What causes ovulation?
29. What happens to an oocyte following ovulation?

## Female Internal Reproductive Organs

The internal accessory organs of the female reproductive system include a pair of uterine tubes, a uterus, and a vagina.

### *Uterine Tubes*

The **uterine tubes** (fallopian tubes or oviducts) open near the ovaries (fig. 19.11). Each tube is about 10 centimeters long and 0.7 centimeters in diameter, passes medially to the uterus, penetrates its wall, and opens into the uterine cavity.

Near each ovary, a uterine tube expands, forming a funnel-shaped *infundibulum* (in″fun-dib′u-lum), which partially encircles the ovary. Fingerlike extensions called *fimbriae* (fim′bre) fringe the infundibulum margin. Although the infundibulum generally does not touch the ovary, one of the larger extensions connects directly to the ovary.

Simple columnar epithelial cells, some *ciliated,* line the uterine tube. The epithelium secretes mucus, and the cilia beat toward the uterus. These actions help draw the secondary oocyte and expelled follicular fluid into the infundibulum following ovulation. Ciliary action and peristaltic contractions of the uterine tube's muscular layer aid transport of the egg down the uterine tube. Fertilization occurs in the uterine tube.

### *Uterus*

The **uterus** receives the embryo that develops from an egg cell fertilized in the uterine tube, and sustains its development. It is a hollow, muscular organ shaped somewhat like an inverted pear.

The size of the uterus changes greatly during pregnancy. In its nonpregnant, adult state, the uterus is about 7 centimeters long, 5 centimeters wide (at its broadest point), and 2.5 centimeters in diameter. The uterus is located medially in the anterior part of the pelvic cavity, superior to the vagina, and usually bends forward over the urinary bladder.

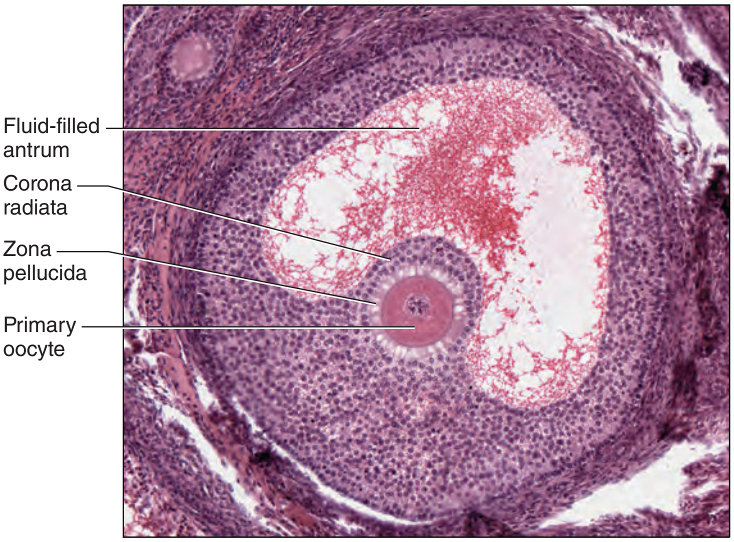

Fluid-filled antrum
Corona radiata
Zona pellucida
Primary oocyte

**FIGURE 19.10** APR Light micrograph of a maturing follicle (250×).

**Q** *Which structure is formed by the follicular cells attached to and surrounding the secondary oocyte.*

**Answer may be found in Appendix F on page 582.**

The upper two-thirds, or *body,* of the uterus has a dome-shaped top called the *fundus* (fig. 19.11). The uterine tubes enter the top of the uterus at its broadest part. The lower third of the uterus is called the **cervix.** This tubular part extends downward into the upper part of the vagina. The cervix surrounds the opening called the *cervical orifice,* through which the uterus opens to the vagina.

The uterine wall is thick and has three layers (figs. 19.11 and 19.12). The **endometrium** (en″do-me′tre-um), the inner mucosal layer, is covered with columnar epithelium and contains abundant tubular glands. The **myometrium** (mi″o-me′tre-um), a thick, middle, muscular layer, consists largely of bundles of smooth muscle fibers. During the monthly female reproductive cycles and during pregnancy, the endometrium and myometrium change extensively. The **perimetrium** (per-ĭ-me′tre-um) consists of an outer serosal layer, which covers the body of the uterus and part of the cervix.

**FACTS OF LIFE** During pregnancy, the uterus expands to 500 times its normal volume.

A precancerous condition, called carcinoma *in situ* (CIS), affects the cervix. It is detected using a *Pap (Papanicolaou) smear test* that identifies cellular changes. Government public health guidelines advise testing annually starting three years after becoming sexually active or by age twenty-one. At age thirty, testing can switch to every three years if no abnormalities have been found. Most cases of CIS do not progress to cancer.

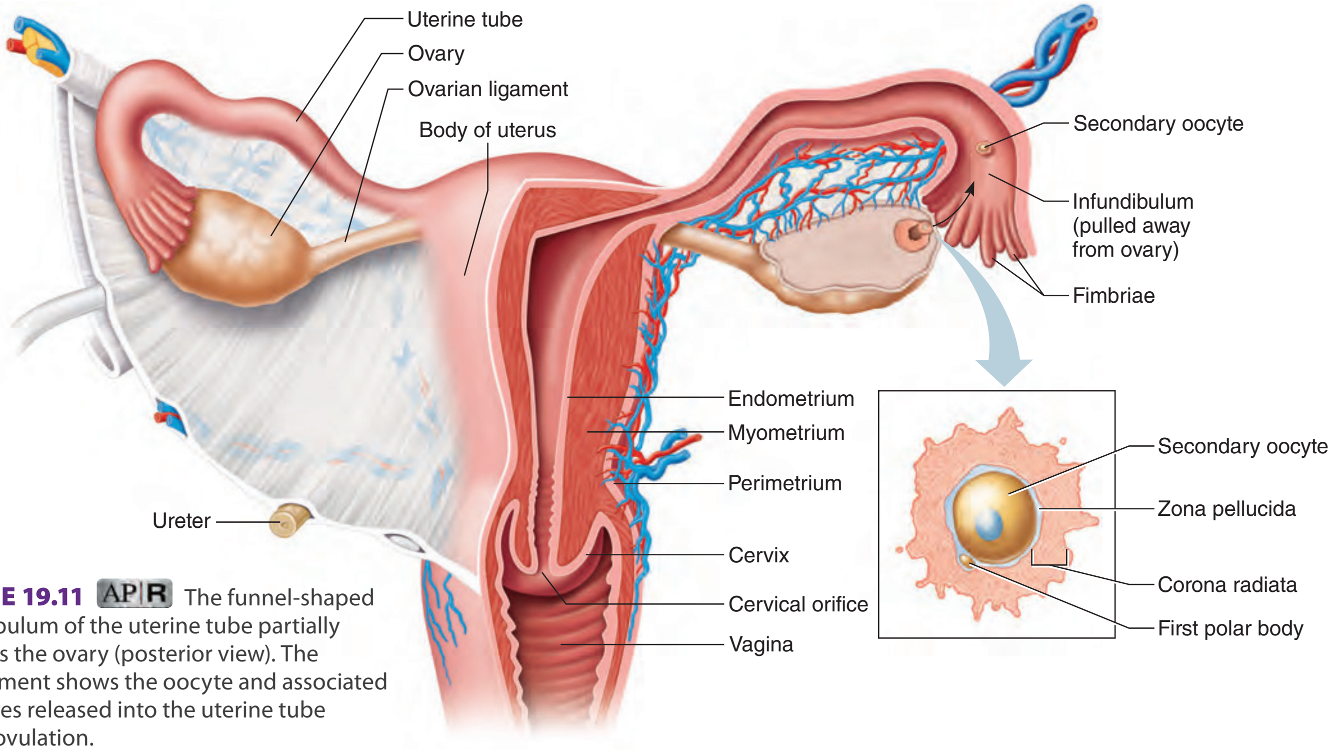

Uterine tube
Ovary
Ovarian ligament
Body of uterus
Secondary oocyte
Infundibulum (pulled away from ovary)
Fimbriae
Endometrium
Myometrium
Perimetrium
Cervix
Cervical orifice
Vagina
Ureter
Secondary oocyte
Zona pellucida
Corona radiata
First polar body

**FIGURE 19.11** APR The funnel-shaped infundibulum of the uterine tube partially encircles the ovary (posterior view). The enlargement shows the oocyte and associated structures released into the uterine tube during ovulation.

### Vagina

The **vagina** is a fibromuscular tube, about 9 centimeters long, extending from the uterus to the outside of the body (see fig. 19.7). It conveys uterine secretions, receives the erect penis during sexual intercourse, and provides an open channel for the offspring to exit the body during birth.

The vagina extends upward and back into the pelvic cavity. It is posterior to the urinary bladder and urethra, anterior to the rectum, and attached to these structures by connective tissues.

A thin membrane of connective tissue and stratified squamous epithelium called the **hymen** partially covers the *vaginal orifice.* A central opening of varying size allows uterine and vaginal secretions to pass to the outside.

The vaginal wall has three layers. The inner *mucosal layer* is stratified squamous epithelium. This layer lacks mucous glands; the mucus in the lumen of the vagina comes from uterine glands and from vestibular glands at the mouth of the vagina.

The middle *muscular layer* mainly consists of smooth muscle fibers. A thin band of striated muscle at the lower end of the vagina helps close the vaginal opening. Another voluntary muscle (bulbospongiosus) is primarily responsible for closing this orifice.

The outer *fibrous layer* consists of dense connective tissue interlaced with elastic fibers. It attaches the vagina to surrounding organs.

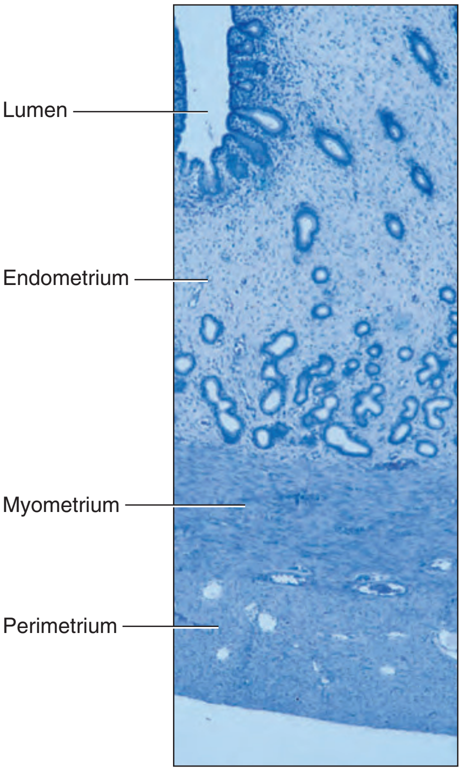


**FIGURE 19.12** APR Light micrograph of the uterine wall (10×).

## PRACTICE

30. How is a secondary oocyte moved along a uterine tube?
31. Describe the structure of the uterus.
32. Describe the structure of the vagina.

## Female External Reproductive Organs

The external accessory organs of the female reproductive system include the labia majora, labia minora, clitoris, and the vestibular glands (see fig. 19.7). These structures that surround the openings of the urethra and vagina compose the **vulva**.

### Labia Majora

The **labia majora** (singular, *labium majus*) enclose and protect the other external reproductive organs. The labia majora correspond to the scrotum of the male and are composed of rounded folds of adipose tissue and a thin layer of smooth muscle, covered by skin.

The labia majora lie close together. A cleft that includes the urethral and vaginal openings separates the labia longitudinally. At their anterior ends, the labia merge to form a medial, rounded elevation of adipose tissue called the *mons pubis,* which overlies the pubic symphysis.

### Labia Minora

The **labia minora** (singular, *labium minus*) are flattened, longitudinal folds between the labia majora (see fig. 19.7). They are composed of connective tissue richly supplied with blood vessels, giving a pinkish appearance. Posteriorly, the labia minora merge with the labia majora, while anteriorly, they converge to form a hoodlike covering around the clitoris.

### Clitoris

The **clitoris** (klit′o-ris) is a small projection at the anterior end of the vulva between the labia minora (see fig. 19.7). In most women it is about 2 centimeters long and 0.5 centimeters in diameter, including a portion embedded in surrounding tissues. The clitoris corresponds to the penis in males and has a similar structure. It is composed of two columns of erectile tissue called *corpora cavernosa.* At its anterior end, a small mass of erectile tissue forms a glans, which is richly supplied with sensory nerve fibers.

### Vestibule

The labia minora enclose a space called the **vestibule.** The vagina opens into the posterior portion of the vestibule, and the urethra opens in the midline, just anterior to the vagina and about 2.5 centimeters posterior to the glans of the clitoris.

A pair of **vestibular glands,** corresponding to the bulbourethral glands in the male, lie one on either side of the vaginal opening. Beneath the mucosa of the vestibule on either side is a mass of vascular erectile tissue called the *vestibular bulb.*

**PRACTICE**

33. What is the male counterpart of the labia majora? Of the clitoris?
34. Which structures are within the vestibule?

### Erection, Lubrication, and Orgasm

Erectile tissues in the clitoris and around the vaginal entrance respond to sexual stimulation. Following such stimulation, parasympathetic impulses from the sacral portion of the spinal cord release the vasodilator nitric oxide (NO), which dilates the arteries associated with the erectile tissues. As a result, blood inflow increases, erectile tissues swell, and the vagina expands and elongates.

If sexual stimulation is sufficiently intense, parasympathetic impulses stimulate the vestibular glands to secrete mucus into the vestibule. This secretion moistens and lubricates the tissues surrounding the vestibule and the lower end of the vagina, facilitating insertion of the penis into the vagina.

The clitoris is abundantly supplied with sensory nerve fibers, which are especially sensitive to local stimulation. Such stimulation culminates in orgasm.

Just prior to orgasm, the tissues of the outer third of the vagina engorge with blood and swell. This increases the friction on the penis during intercourse. Orgasm initiates a series of reflexes involving the sacral and lumbar parts of the spinal cord. In response to these reflexes, the muscles of the perineum and the walls of the uterus and uterine tubes contract rhythmically. These contractions help transport sperm cells through the female reproductive tract toward the upper ends of the uterine tubes. Table 19.2 summarizes the functions of the female reproductive organs.

**PRACTICE**

35. What events result from parasympathetic stimulation of the female reproductive organs?
36. What changes occur in the vagina just prior to and during orgasm?

## 19.5 Hormonal Control of Female Reproductive Functions

The hypothalamus, the anterior pituitary gland, and the ovaries secrete hormones that control maturation of female sex cells, the development and maintenance of female secondary sex characteristics, and changes that occur during the reproductive cycle.

**TABLE 19.2 Functions of the Female Reproductive Organs** APR

| Organ | Function |
|---|---|
| Ovary | Produces oocytes and female sex hormones |
| Uterine tube | Conveys secondary oocyte toward uterus; site of fertilization; conveys developing embryo to uterus |
| Uterus | Protects and sustains embryo during pregnancy |
| Vagina | Conveys uterine secretions to outside of body; receives erect penis during sexual intercourse; provides open channel for offspring during birth process |
| Labia majora | Enclose and protect other external reproductive organs |
| Labia minora | Form margins of vestibule; protect openings of vagina and urethra |
| Clitoris | Produces feelings of pleasure during sexual stimulation due to abundant sensory nerve endings in glans |
| Vestibule | Space between labia minora that contains vaginal and urethral openings |
| Vestibular glands | Secrete fluid that moistens and lubricates vestibule |

### Female Sex Hormones

The female body is reproductively immature until about ten years of age. Then, the hypothalamus begins to secrete increasing amounts of GnRH, which, in turn, stimulates the anterior pituitary to release the gonadotropins FSH and LH. These hormones play primary roles in controlling female sex cell maturation and in producing female sex hormones (fig. 19.13).

Several tissues, including the ovaries, the adrenal cortices, and the placenta (during pregnancy), secrete female sex hormones belonging to two major groups—**estrogens** (es′tro-jenz) and **progesterone** (pro-jes′tĭ-rōn). *Estradiol* is the most abundant of the estrogens, which also include *estrone* and *estriol.*

The ovaries are the primary source of estrogens (in a nonpregnant female). At puberty, under the influence of the anterior pituitary, the ovaries secrete increasing amounts of estrogens. Estrogens stimulate enlargement of accessory organs, including the vagina, uterus, uterine tubes, ovaries, and external reproductive structures. Estrogens also develop and maintain the *female secondary sex characteristics,* which include (fig. 19.13):

1. development of the breasts and the ductile system of the mammary glands in the breasts.
2. increased deposition of adipose tissue in the subcutaneous layer generally and in the breasts, thighs, and buttocks particularly.
3. increased vascularization of the skin.

The ovaries are also the primary source of progesterone (in a nonpregnant female). This hormone promotes changes in the uterus during the female reproductive cycle, affects the mammary glands, and helps regulate the secretion of gonadotropins from the anterior pituitary gland.

Androgen (male sex hormone) concentrations produce certain other changes in females at puberty. For example, increased hair growth in the pubic and axillary regions is due to androgen secreted by the adrenal cortices. Conversely, development of the female skeletal configuration, which includes narrow shoulders and broad hips, is a response to a low androgen concentration.

## PRACTICE

37. What stimulates sexual maturation in a female?
38. What is the function of estrogens?
39. What is the function of androgen in a female?

## Female Reproductive Cycle

The female reproductive cycle is characterized by regular, recurring changes in the endometrium, which culminate in menstrual bleeding (menses). Such cycles usually begin around age thirteen and continue into the early fifties, then cease.

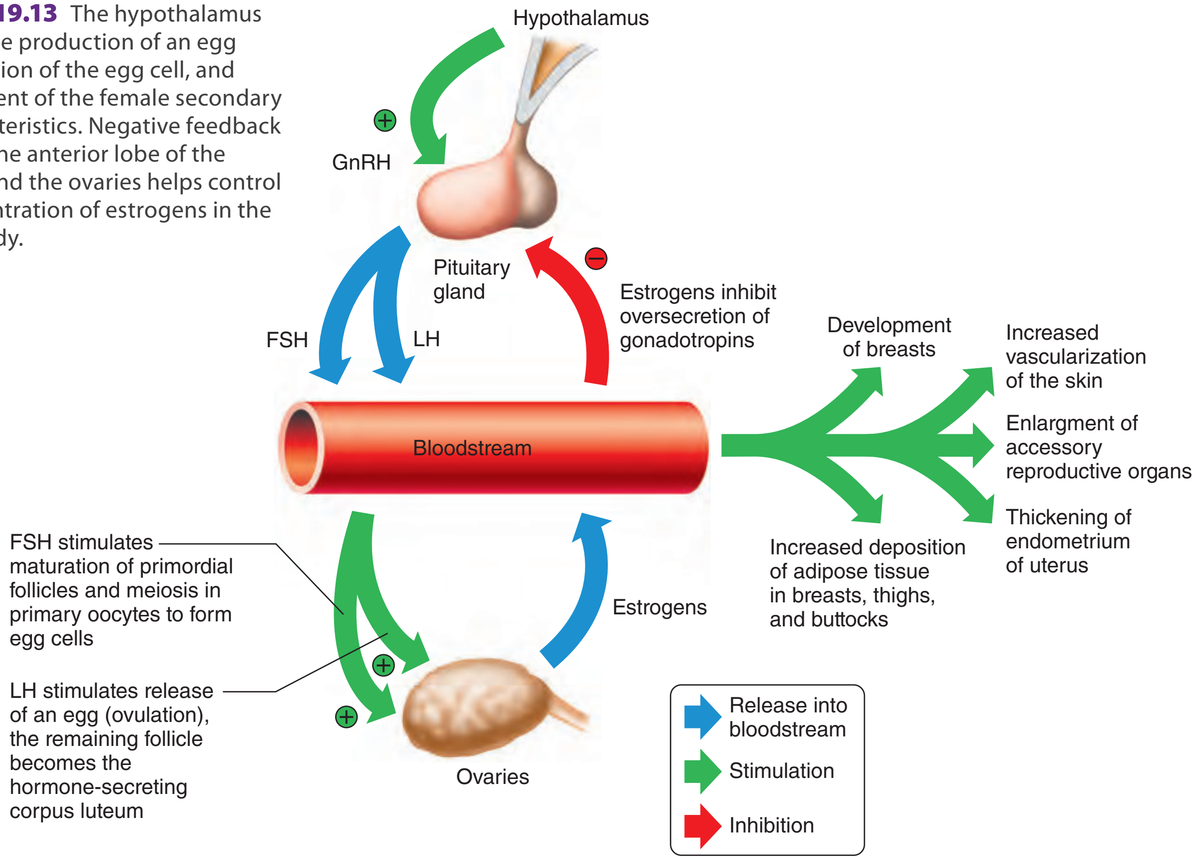
A female's first reproductive cycle, called **menarche** (mĕ-nar′ke), occurs after the ovaries and other organs of the reproductive control system mature and begin responding to certain hormones. Then, the hypothalamic secretion of GnRH stimulates the anterior pituitary to release threshold levels of FSH and LH. FSH stimulates the final maturation of an ovarian follicle. The follicular cells produce increasing amounts of estrogens and some progesterone. LH stimulates certain ovarian cells to secrete precursor molecules (such as testosterone), also used to produce estrogens.

In a young female, estrogens stimulate the development of secondary sex characteristics. Estrogens secreted during subsequent reproductive cycles continue the development and maintenance of these characteristics.

Increasing concentration of estrogens during the first week or so of a reproductive cycle changes the uterine lining, thickening the glandular endometrium (proliferative phase). Meanwhile, the follicle fully matures, and by around the fourteenth day of the cycle, the antral follicle appears on the ovary surface as a blisterlike bulge. Within the follicle, the follicular cells, which surround and connect the secondary oocyte to the inner wall, loosen. Follicular fluid accumulates.

While the follicle matures, it secretes estrogens that inhibit the release of LH from the anterior pituitary gland but allow LH to be stored in the gland. Estrogens also make anterior pituitary cells more sensitive to the

**FIGURE 19.13** The hypothalamus controls the production of an egg cell, ovulation of the egg cell, and development of the female secondary sex characteristics. Negative feedback between the anterior lobe of the pituitary and the ovaries helps control the concentration of estrogens in the female body.


Hypothalamus
+
GnRH
Pituitary gland
FSH
LH
−
Estrogens inhibit oversecretion of gonadotropins
Bloodstream
Development of breasts
Increased vascularization of the skin
Enlargment of accessory reproductive organs
Thickening of endometrium of uterus
Increased deposition of adipose tissue in breasts, thighs, and buttocks
FSH stimulates maturation of primordial follicles and meiosis in primary oocytes to form egg cells
LH stimulates release of an egg (ovulation), the remaining follicle becomes the hormone-secreting corpus luteum
+
+
Estrogens
Ovaries
Release into bloodstream
Stimulation
Inhibition

action of GnRH, which is released from the hypothalamus in rhythmic pulses about ninety minutes apart.

Near the fourteenth day of follicular development, the anterior pituitary cells finally respond to the pulses of GnRH and release the stored LH. The resulting surge in LH concentration lasts about thirty-six hours. In response to the LH, the primary oocyte completes meiosis I. The LH surge also leads to weakening and rupturing of the bulging follicular wall. This event sends the secondary oocyte and follicular fluid out of the ovary (ovulation).

Following ovulation, the space containing the follicular fluid fills with blood, which soon clots. Under the influence of LH, the remnants of the follicle within the ovary form a temporary glandular structure called a **corpus luteum** (kor′pus loot′e-um) ("yellow body") (see fig. 19.9).

Follicular cells secrete some progesterone during the first part of the reproductive cycle. However, corpus luteum cells secrete abundant progesterone and estrogens during the second half of the cycle. Consequently, as a corpus luteum forms, the blood progesterone concentration sharply increases.

Progesterone causes the endometrium to become more vascular and glandular. It also stimulates the uterine glands to secrete more glycogen and lipids (secretory phase). The endometrial tissues fill with fluids containing nutrients and electrolytes, which provide a favorable environment for an embryo to develop.

High levels of estrogens and progesterone inhibit the anterior pituitary gland's release of LH and FSH. Consequently, no other follicles are stimulated to complete maturation when the corpus luteum is active. However, if the secondary oocyte released at ovulation is not fertilized, the corpus luteum begins to degenerate (regress) on about the twenty-fourth day of the cycle. Eventually, connective tissue replaces it. The remnant of such a corpus luteum is called a *corpus albicans* (see fig. 19.9).

When the corpus luteum ceases to function, concentrations of estrogens and progesterone rapidly decline, and in response, blood vessels in the endometrium constrict. This reduces the supply of oxygen and nutrients to the thickened endometrium (stratum functionalis and stratum basalis), and these lining tissues soon disintegrate and slough off. At the same time, blood leaves damaged capillaries, creating a flow of blood and cellular debris that passes through the vagina as the *menstrual flow* (menses). This flow usually begins about the twenty-eighth day of the cycle and continues for three to five days, while the concentrations of estrogens are relatively low. The beginning of the menstrual flow marks the end of a reproductive cycle and the beginning of a new cycle as a new developing antral follicle becomes available. This cycle is summarized in table 19.3 and diagrammed in figure 19.14.

Low blood concentrations of estrogens and progesterone at the beginning of the reproductive cycle mean that the hypothalamus and anterior pituitary gland are no longer inhibited. Consequently, FSH and LH concentrations soon increase, stimulating a new antral follicle to mature. As this follicle secretes estrogens, the uterine lining undergoes repair, and the endometrium begins to thicken again.

Elite female athletes and professional dancers may have disturbed reproductive cycles, ranging from diminished menstrual flow (oligomenorrhea) to complete stoppage (amenorrhea). The more active an athlete or dancer, the more likely it is that she will have menstrual irregularities, and this may impair her ability to conceive. Trim elite athletes and dancers have little fat, leading to decreased secretion of the hormone leptin. Decreased leptin secretion is associated with lowered secretion of gonadotropin-releasing hormone from the hypothalamus, which in turn lowers the blood estrogen level. Adipose tissue itself also produces some estrogen. Adequate estrogen is necessary for fertility. These girls and women are also at high risk of developing low bone density and cardiovascular impairments.

## Menopause

After puberty, reproductive cycles continue at regular intervals into the late forties or early fifties, when the ovaries start to produce lower amounts of estrogen and

**TABLE 19.3 Major Events in a Reproductive Cycle**

1. The anterior pituitary gland secretes follicle-stimulating hormone (FSH) and luteinizing hormone (LH).
2. FSH stimulates maturation of a dominant follicle.
3. Follicular cells produce and secrete estrogens.
    a. Estrogens maintain secondary sex characteristics.
    b. Estrogens cause the endometrium to thicken.
4. The anterior pituitary releases a surge of LH, which leads to ovulation.
5. Follicular cells become corpus luteum cells, which secrete estrogens and progesterone.
    a. Estrogens continue to stimulate uterine wall development.
    b. Progesterone stimulates the endometrium to become more glandular and vascular.
    c. Estrogens and progesterone inhibit the secretion of FSH and LH from the anterior pituitary gland.
6. If the secondary oocyte is not fertilized, the corpus luteum degenerates and no longer secretes estrogens and progesterone.
7. As the concentrations of estrogens and progesterone decline, blood vessels in the endometrium constrict.
8. The uterine lining disintegrates and sloughs off, producing a menstrual flow.
9. The anterior pituitary gland is no longer inhibited and again secretes FSH and LH.
10. The reproductive cycle repeats.

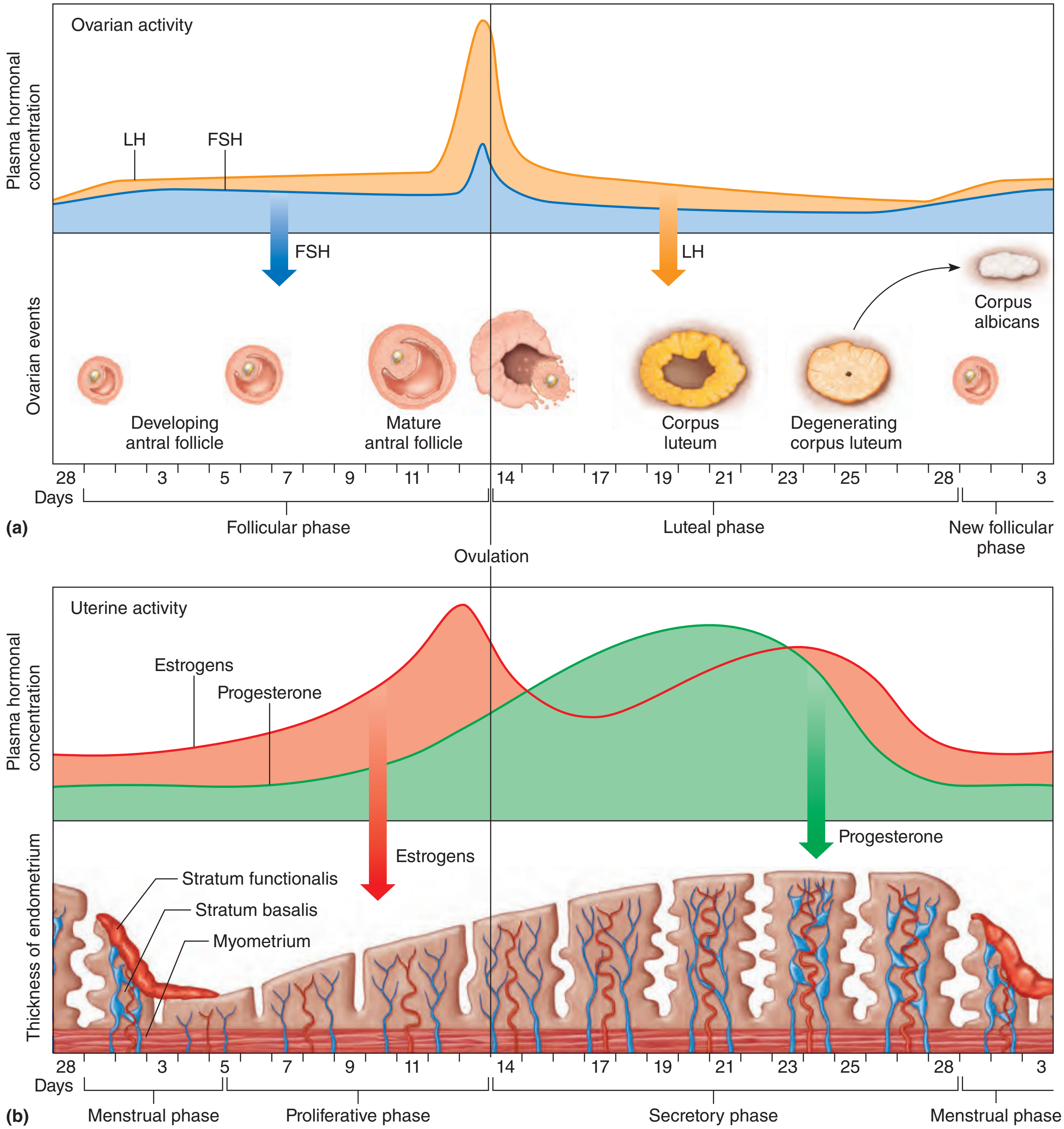

Plasma hormonal concentration
Ovarian activity
LH
FSH
FSH
LH
Ovarian events
Developing antral follicle
Mature antral follicle
Corpus luteum
Degenerating corpus luteum
Corpus albicans
28
3
5
7
9
11
14
17
19
21
23
25
28
3
Days
(a)
Follicular phase
Luteal phase
New follicular phase
Ovulation
Plasma hormonal concentration
Uterine activity
Estrogens
Progesterone
Estrogens
Progesterone
Thickness of endometrium
Stratum functionalis
Stratum basalis
Myometrium
28
3
5
7
9
11
14
17
19
21
23
25
28
3
Days
(b)
Menstrual phase
Proliferative phase
Secretory phase
Menstrual phase

**FIGURE 19.14** APR Major events in the female reproductive cycle. (**a**) Plasma hormonal concentrations of FSH and LH affect follicle maturation in the ovaries. (**b**) Plasma hormonal concentrations of estrogen and progesterone influence changes in the uterine lining.

progesterone. This results in the reproductive cycles becoming less predictable. Then, within a few months or years, the cycles cease. This period in life is called **menopause** (men′o-pawz), or female climacteric.

Reduced concentrations of estrogens and lack of progesterone may change the female secondary sex characteristics. The breasts, vagina, uterus, and uterine tubes may shrink, and the pubic and axillary hair may thin.

## PRACTICE

40. Trace the events of the female reproductive cycle.
41. What causes menstrual flow?
42. What are some changes that may occur at menopause?

## 19.6 | Mammary Glands

The **mammary glands** are accessory organs of the female reproductive system specialized to secrete milk following pregnancy. They are in the subcutaneous tissue of the anterior thorax within elevations called *breasts* (fig. 19.15*a*; reference plate 1, p. 32). The breasts overlie the *pectoralis major* muscles and extend from the second to the sixth ribs and from the sternum to the axillae.

A *nipple* is located near the tip of each breast at about the level of the fourth intercostal space. A circular area of pigmented skin, called the *areola,* surrounds each nipple (fig. 19.15*b*).

A mammary gland is composed of fifteen to twenty lobes. Each lobe contains glands (alveolar glands), drained by alveolar ducts, which drain into a lactiferous duct, that leads to the nipple and opens to the outside (fig. 19.15). Dense connective and adipose tissues separate the lobes. These tissues also support the glands and attach them to the fascia of the underlying pectoral muscles. Other connective tissue, which forms dense strands called *suspensory ligaments,* extends inward from the dermis of the breast to the fascia, helping support the breast.

The mammary glands of males and females are similar. As children reach puberty, the glands in males do not develop, whereas ovarian hormones stimulate development of the glands in females. The alveolar glands and ducts enlarge, and fat is deposited around and within the breasts. Chapter 20 (pp. 565–566) describes the hormonal mechanism that stimulates mammary glands to produce and secrete milk. Clinical Application 19.3 discusses diagnosis, treatment, and prevention of breast cancer.

**PRACTICE**

43. Describe the structure of a mammary gland.
44. How does ovarian hormone secretion change the mammary glands?

## 19.7 | Birth Control

*Birth control* is the voluntary regulation of the number of offspring produced and the time they are conceived. This control requires a method of **contraception** (kon″trah-sep′shun) designed to avoid fertilization of an egg cell following sexual intercourse (coitus) or to prevent implantation of a hollow ball of cells (a blastocyst) that will develop into an embryo. The several methods of contraception have varying degrees of effectiveness.

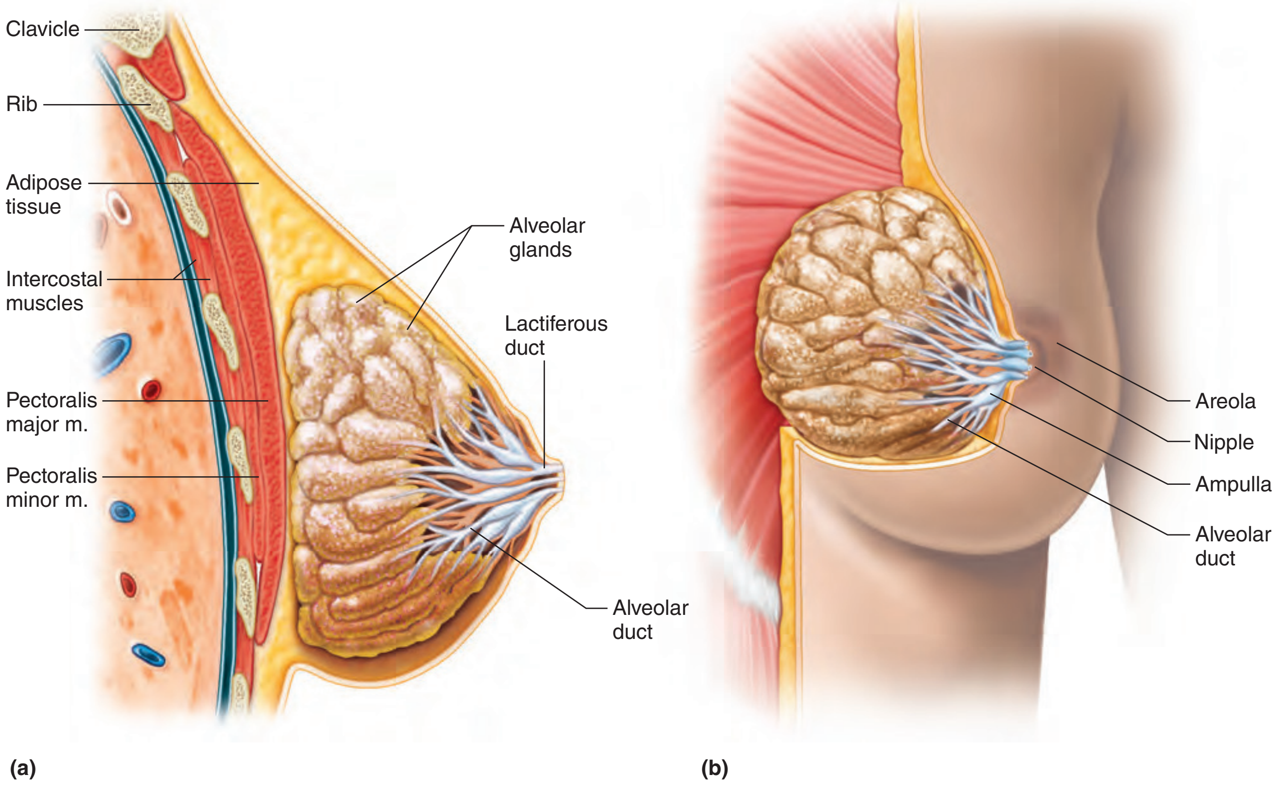


**FIGURE 19.15** APR Structure of the female breast and mammary glands. (**a**) Sagittal section. (**b**) Anterior view. (*m.* stands for *muscle.*)

## Coitus Interruptus

*Coitus interruptus* is the practice of withdrawing the penis from the vagina before ejaculation, preventing entry of sperm cells into the female reproductive tract. This method can still result in pregnancy because a male may find it difficult to withdraw just prior to ejaculation. Also, some semen containing sperm cells may reach the vagina before ejaculation occurs.

## Rhythm Method

The *rhythm method* (also called timed coitus or natural family planning) requires abstinence from sexual intercourse two days before and one day after ovulation. The rhythm method results in a relatively high rate of pregnancy because accurately identifying infertile ("safe") times to have intercourse is difficult. Another disadvantage of the rhythm method is that it requires adherence to a particular pattern of behavior and restricts spontaneity in sexual activity.

## Mechanical Barriers

*Mechanical barrier* contraceptives prevent sperm cells from entering the female reproductive tract during sexual intercourse. The *male condom* is a thin latex or natural membrane sheath placed over the erect penis before intercourse to prevent semen from entering the vagina upon ejaculation (fig. 19.16*a*). A *female condom* resembles a small plastic bag. A woman inserts it into her vagina prior to intercourse. The device blocks sperm cells from reaching the cervix (fig. 19.16*a*).

Some men feel that a condom decreases the sensitivity of the penis during intercourse, and condom use may interrupt spontaneity. However, condoms are inexpensive and may also protect the user from contracting or spreading some sexually transmitted infections.

Another mechanical barrier is the *diaphragm*, a cup-shaped device with a flexible ring forming the rim. The diaphragm is inserted into the vagina so that it covers the cervix, preventing sperm cells from entering the

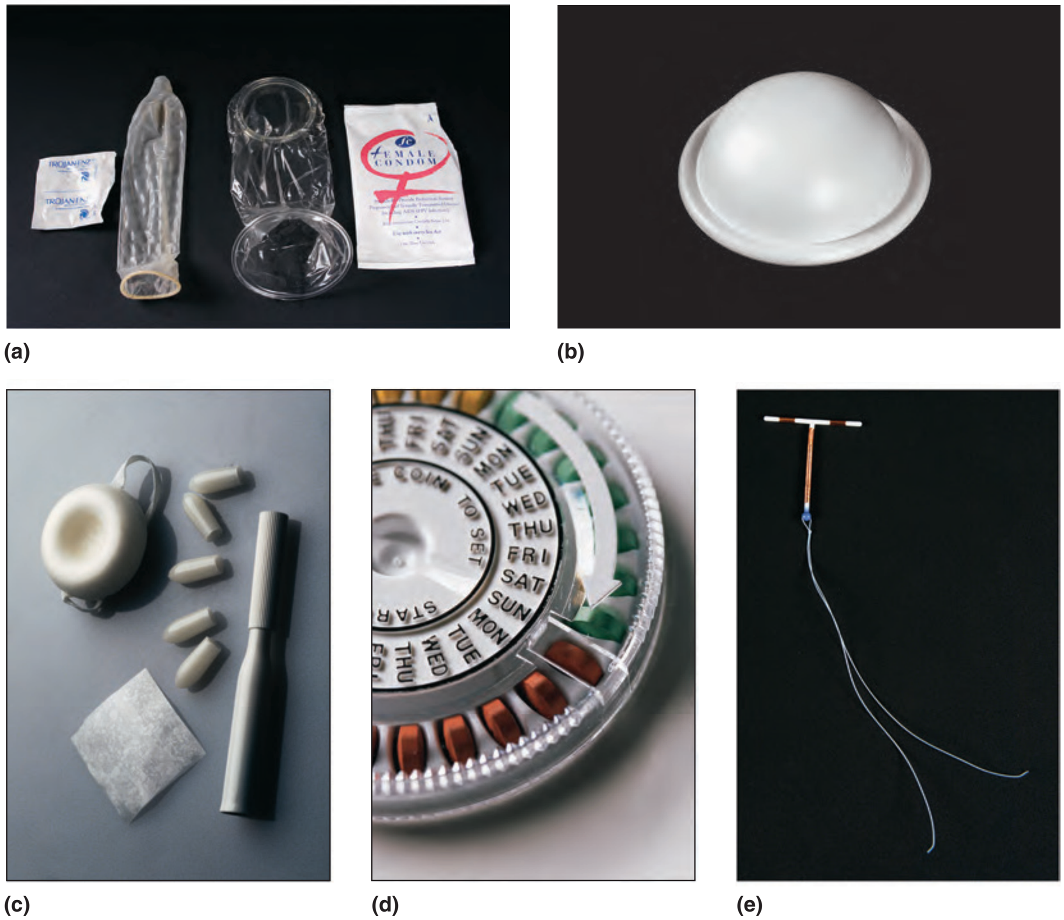


**FIGURE 19.16** Devices and substances used for birth control include (**a**) male and female condoms, (**b**) a diaphragm, (**c**) spermicide in film, sponge, suppositories, and gel, (**d**) oral contraceptives, and (**e**) a copper IUD.

**Q** *Which of these methods of birth control, employing combined hormone therapy, is statistically very effective?*
**Answer may be found in Appendix F on page 582.**

## CLINICAL APPLICATION 19.3

## Treating Breast Cancer

As a woman becomes older, her chance of developing breast cancer approaches one in eight (table 19B). About 1% of breast cancer cases are in men. There are several varieties of breast cancer, distinguished by the types of cells affected and by certain mutations that increase susceptibility to the condition. As research reveals the cellular and molecular characteristics that distinguish subtypes of the disease, treatments are being increasingly tailored to individuals. This approach may delay disease progression and increase survival rate, while enabling patients to avoid drugs that will not work.

### Warning Signs

Changes that could signal breast cancer include a small area of thickened tissue; a dimple; a change in contour; or a nipple that is flattened, points in an unusual direction, or produces a discharge. A woman can note these changes by performing a monthly "breast self-exam," in which she lies flat on her back with an arm raised behind her head and systematically feels all parts of each breast. But sometimes breast cancer gives no warning—fatigue and feeling ill may not occur until the disease has spread beyond the breast.

After finding a lump, the next step is a physical exam, where a health-care provider palpates the breast and does a mammogram, which is an X-ray scan that can pinpoint the location and approximate extent of abnormal tissue (fig. 19B). An ultrasound scan can distinguish between a cyst (a fluid-filled sac of glandular tissue) and a tumor (a solid mass). If an area is suspicious, a thin needle is used to take a biopsy (sample) of the tissue, whose cells are scrutinized under a microscope for the characteristics of cancer.

**TABLE 19B** **Breast Cancer Risk**

| By Age | Odds | By Age | Odds |
|---|---|---|---|
| 25 | 1 in 19,608 | 60 | 1 in 24 |
| 30 | 1 in 2,525 | 65 | 1 in 17 |
| 35 | 1 in 622 | 70 | 1 in 14 |
| 40 | 1 in 217 | 75 | 1 in 11 |
| 45 | 1 in 93 | 80 | 1 in 10 |
| 50 | 1 in 50 | 85 | 1 in 9 |
| 55 | 1 in 33 | 95 or older | 1 in 8 |

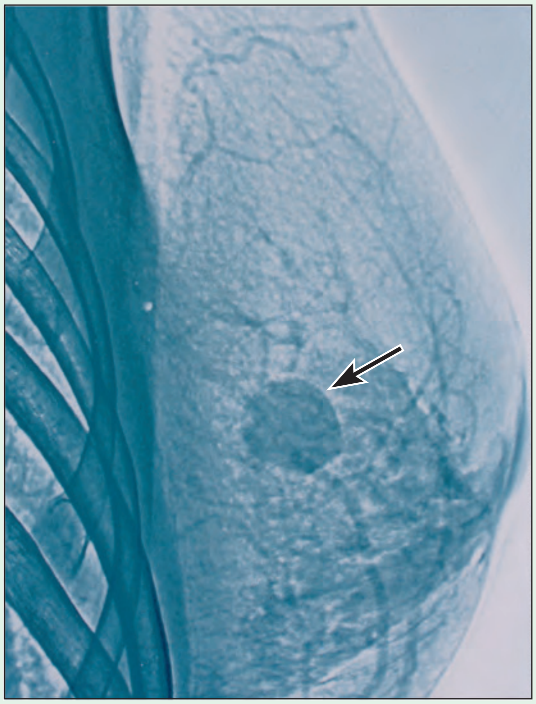


**FIGURE 19B** APR Mammogram of a breast with a tumor (arrow).

uterus (fig. 19.16*b*). To be effective, a diaphragm must be fitted for size by a physician, inserted properly, and used with a spermicide applied to the diaphragm surface adjacent to the cervix and to the rim of the diaphragm. The device must be left in position for several hours following sexual intercourse. A diaphragm can be inserted up to six hours prior to sexual contact.

Similar to but smaller than the diaphragm is the *cervical cap,* which must also be fitted by a physician. A woman inserts it with her fingers before intercourse. For centuries, different societies have used cervical caps made of such varied substances as beeswax, lemon halves, paper, and opium poppy fibers. The cervical shield, which does not need fitting, has a one-way valve that creates suction against the cervix.

## Chemical Barriers

*Chemical barrier* contraceptives include creams, foams, and jellies with spermicidal properties (fig. 19.16*c*). These chemicals create an unfavorable environment in the vagina for sperm cells.

Chemical barrier contraceptives are fairly easy to use but have a high failure rate when used alone. They

Further tests can identify estrogen and progesterone receptors on cancer cells, providing information used to guide treatment choices. A very aggressive form of breast cancer is called triple negative, because affected cells do not have receptors (for estrogen, progesterone, and epidermal growth factor) that many chemotherapies target. Triple negative breast cancer tends to start earlier, spread faster, and recur more often than other types.

### Surgery, Radiation, and Chemotherapies

If biopsied breast cells are cancerous, treatment usually begins with surgery. A lumpectomy removes a small tumor and some surrounding tissue; a simple mastectomy removes a breast; and a modified radical mastectomy removes the breast and usually one or two lymph nodes, but preserves the pectoral muscles. If cancer cells are detected in the lymph nodes further surgery is performed.

Many breast cancers are then treated with radiation and combinations of chemotherapeutic drugs, plus sometimes newer drugs that are targeted to certain types of breast cancer. Standard chemotherapies kill all rapidly dividing cells, and those used for breast cancer include fluorouracil, doxorubicin, cyclophosphamide, methotrexate, and paclitaxol. Protocols that provide more frequent, lower doses can temper some of the side effects of these powerful drugs.

Newer treatments are easier to tolerate and can be extremely effective. Three types of drugs keep signals (estrogen and growth factors) from stimulating cancer cells to divide:

1. Selective estrogen receptor modulators (SERMs), such as tamoxifen and raloxifene, block estrogen receptors. About half of people with breast cancer have receptors for estrogen on their cancer cells and can benefit from these drugs.
2. Aromatase inhibitors block an enzyme required for tissues other than those of the ovaries to synthesize estrogens. These drugs are used in women who are past menopause, whose ovaries no longer synthesize estrogen. They are prescribed after a five-year course of a SERM.
3. Herceptin (trastuzumab) can help people whose cancer cells bear too many receptors that bind epidermal growth factor. It is a monoclonal antibody, based on an immune system protein. Herceptin blocks the growth factor from signaling cell division. This drug treats a particularly aggressive form of the disease that strikes younger women.

### Prevention Strategies

Public health agencies and physicians are debating the exact age at which women should begin having mammograms, and how frequently they should have them thereafter. For this reason, it is important for women to discuss personal mammogram schedules with health-care providers familiar with their family histories. Although a mammogram can detect a tumor up to two years before it can be felt, it can also miss some tumors. Thus, breast self-exam is also important in early detection.

Genetic tests can identify women who have inherited certain variants of genes—such as *BRCA1, BRCA2, p53,* and *HER-2/neu*—that place them at high risk for developing breast cancer. Some of these women have their breasts removed to prevent the disease. Gene expression profiling (determining which genes are turned on or off in cancer cells) can determine which drugs are most likely to help particular patients, and estimate risk of recurrence after surgery. This type of information may help decide on follow-up treatment.

Only 5% to 10% of all breast cancers arise from an inherited tendency. Much research seeks to identify the environmental triggers that contribute to causing the majority of cases.

are more effective when used with a condom or diaphragm. The contraceptive sponge contains a spermicide and blocks entry of sperm into the uterus.

## Combined Hormone Contraceptives

Combined hormone contraceptives deliver estrogen and progestin to prevent pregnancy. Various methods are used to administer the hormones, but all work on the same principle with about the same efficacy, although the amounts of the component hormones may vary. One such method is a small flexible chemical ring inserted deep into the vagina once a month, remaining in place three out of four weeks. A plastic patch impregnated with the hormones may be applied to the skin on the buttocks, stomach, arm, or upper torso once a week for three out of four weeks. The most commonly used method to deliver the hormones is orally, in pill form (fig. 19.16*d*).

Combined hormone contraceptives contain synthetic estrogen-like and progesterone-like chemicals. These drugs disrupt the normal pattern of gonadotropin (FSH and LH) secretion, preventing follicle maturation and the LH surge that leads to ovulation. They also thicken cervical mucus to prevent the sperm from joining an egg. Most combined hormone contraceptives cause light monthly bleeding. A new type of pill causes only four bleeding periods a year.

If used correctly, combined hormone contraceptives prevent pregnancy nearly 100% of the time. However, they may cause nausea, retention of body fluids, increased skin pigmentation, and breast tenderness. Some women, particularly those over thirty-five years of age who smoke, may develop intravascular blood clots, liver disorders, or high blood pressure when using certain types of these contraceptives.

## Other Hormone Contraceptives

An intramuscular injection of medroxyprogesterone acetate protects against pregnancy for three months by preventing follicle maturation and release of a secondary oocyte. It also alters the cervix to prevent the sperm from joining an egg. Medroxyprogesterone acetate is long-acting; it takes ten to eighteen months after the last injection for the effects to wear off. Use of this drug requires a doctor's care because of potential side effects and risks.

An implantable rod containing progestin may be inserted under the skin of the arm. This hormone insert also prevents follicle maturation and ovulation for up to three years.

## Intrauterine Devices

An *intrauterine device (IUD)* is a small, solid object that a physician places in the uterine cavity (fig. 19.16*e*). A copper-containing IUD interferes with fertilization and implantation of a blastocyst, perhaps by inflaming the uterine tissues, for up to ten years. A levonorgestrel-releasing IUD, combining hormone contraception with an IUD, is effective in preventing pregnancy for up to five years.

An IUD may be spontaneously expelled from the uterus, or produce abdominal pain or excessive menstrual bleeding. It may also harm the uterus or produce other serious health problems.

## Sterilization

Surgical methods of contraception sterilize the male or female. In the male, a physician removes a small section of each ductus (vas) deferens near the epididymis and ties (ligates) the cut ends of the ducts (fig. 19.17*a*). This is a *vasectomy*, an operation that produces few side effects, although it may cause some pain for a week or two.

After a vasectomy, sperm cells cannot leave the epididymis; thus, they are excluded from the semen. However, sperm cells may already be present in the ducts distal to the cuts. Consequently, the sperm count may not reach zero for several weeks.

The corresponding procedure in the female is *tubal ligation* (fig. 19.17*b*). The uterine tubes are cut and ligated so that sperm cells cannot reach an egg cell. A nonsurgical method of sterilization involves the use of a tube inserted through the vagina and uterus, then into the uterine tubes to deliver a tiny spring-like device. Within three months, scar tissue blocks the uterine tubes so sperm cannot reach the egg to fertilize it.

Sterilization procedures do not change hormonal concentrations or sex drives. These procedures are the most reliable forms of contraception. Reversing them requires microsurgery.

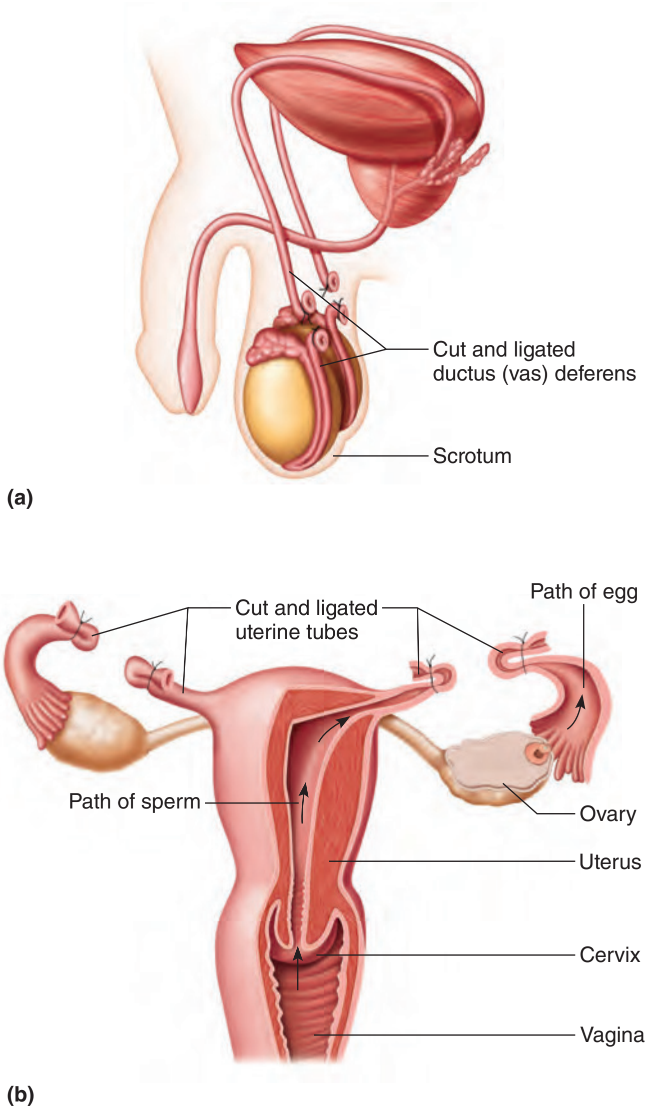

Cut and ligated ductus (vas) deferens
Scrotum
(a)
Cut and ligated uterine tubes
Path of egg
Path of sperm
Ovary
Uterus
Cervix
Vagina
(b)

**FIGURE 19.17** Surgical methods of birth control. (**a**) In a vasectomy, each ductus (vas) deferens is cut and ligated. (**b**) In a tubal ligation, each uterine tube is cut and ligated.

## PRACTICE

45. What factors make the rhythm method less reliable than some other methods of contraception?
46. Describe two methods of contraception that use mechanical barriers.
47. How do combined hormone contraceptives prevent pregnancy?
48. How does an IUD prevent pregnancy?

## 19.8 Sexually Transmitted Infections

The term **sexually transmitted infection (STI)** is replacing the term *sexually transmitted disease (STD)* because a person can be infected with a pathogen and transmit the pathogen to others but not develop the symptoms of the disease. By the time symptoms appear, it is often too late to prevent complications or spread of the infection to sexual partners. Many diseases associated with STIs have similar symptoms, and some of the symptoms are also seen in diseases or allergies not sexually related, so it is wise to consult a physician if one or a combination of these symptoms appears:

1. burning sensation during urination.
2. pain in the lower abdomen.
3. fever or swollen glands in the neck.
4. discharge from the vagina or penis.
5. pain, itching, or inflammation in the genital or anal area.
6. pain during intercourse.
7. sores, blisters, bumps, or a rash anywhere on the body, particularly the mouth or genitals.
8. itchy, runny eyes.

Table 19.4 describes some prevalent STIs. One possible complication of the associated diseases gonorrhea and chlamydia is **pelvic inflammatory disease,** in which bacteria enter the vagina and spread throughout the reproductive organs. The disease begins with intermittent cramps, followed by sudden fever, chills, weakness, and severe cramps. Hospitalization and intravenous antibiotics can stop the infection. The uterus and uterine tubes are often scarred, resulting in infertility and increased risk of ectopic pregnancy, in which the embryo develops in a uterine tube.

*Acquired immune deficiency syndrome (AIDS)* is a steady deterioration of the body's immune defenses in which the body is overrun by infection and often cancer. The human immunodeficiency virus (HIV) that causes AIDS is transmitted in body fluids such as semen, blood, and milk. It is most frequently passed during unprotected intercourse or by using a needle containing contaminated blood. Clinical Application 14.1 (p. 399) explores HIV infection further.

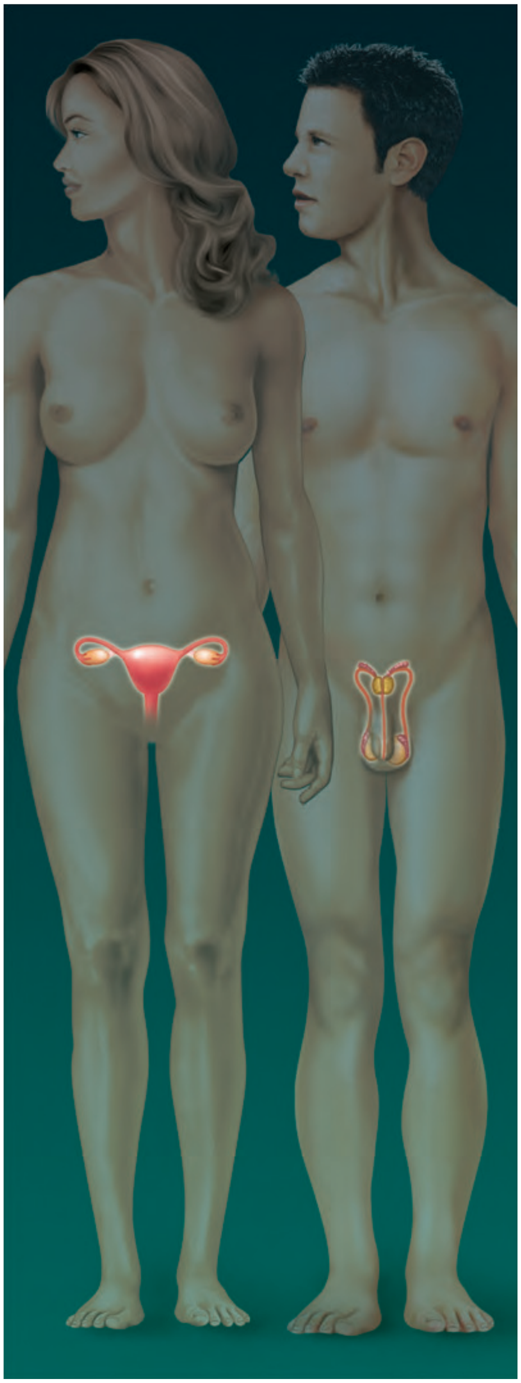
## PRACTICE

49. Why is the term sexually transmitted infection replacing the term sexually transmitted disease?
50. What are some common symptoms of diseases associated with sexually transmitted infections?

**TABLE 19.4** Some Sexually Transmitted Infections

| Associated Disease | Cause | Symptoms | Treatment |
|---|---|---|---|
| Acquired immune deficiency syndrome | Human immunodeficiency virus | Fever, weakness, infections, cancer | Drugs to treat or delay symptoms |
| Chlamydia infection | *Chlamydia trachomatis* bacteria | Painful urination and intercourse, mucous discharge from penis or vagina | Antibiotics |
| Genital herpes | Herpes simplex 2 virus | Genital sores, fever | Antiviral drug (acyclovir) |
| Genital warts | Human papilloma virus | Warts on genitals | Chemical or surgical removal |
| Gonorrhea | *Neisseria gonorrhoeae* bacteria | In women, usually none; in men, painful urination | Antibiotics |
| Syphilis | *Treponema pallidum* bacteria | Initial chancre usually on genitals or mouth; rash six months later; several years with no symptoms as infection spreads; finally damage to heart, liver, nerves, brain | Antibiotics |

# Reproductive Systems



Gamete production, fertilization, fetal development, and childbirth are essential for survival of the species.

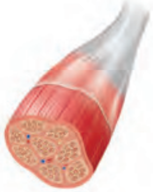
## Integumentary System

Skin sensory receptors play a role in sexual pleasure.

## Skeletal System

Bones can be a temporary source of calcium during lactation.

## Muscular System



Skeletal, cardiac, and smooth muscles all play a role in reproductive processes and sexual activity.

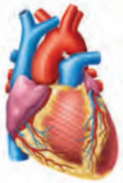
## Nervous System

The nervous system plays a major role in sexual activity and sexual pleasure.

## Endocrine System

Hormones control the production of eggs in the female and sperm in the male.

## Cardiovascular System



Blood pressure is necessary for the normal function of erectile tissue in the male and female.

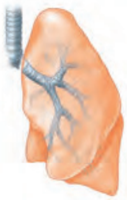
## Lymphatic System

Special mechanisms inhibit the female immune system from attacking sperm as foreign invaders.

## Digestive System

Proper nutrition is essential for the formation of normal gametes.

## Respiratory System



Breathing provides oxygen that assists in the production of ATP needed for egg and sperm development.

## Urinary System

Male urinary and reproductive systems share structures. Kidneys help compensate for fluid loss from the reproductive systems.

## Summary Outline

### 19.1 Introduction (p. 519)

*Reproductive organs produce sex cells and sex hormones, nurture these cells, or transport them.*

### 19.2 Organs of the Male Reproductive System (p. 519)

*The primary male sex organs are the testes, which produce sperm cells and male sex hormones. Accessory sex organs are internal and external.*

1. Testes
    a. Structure of the testes
        (1) The testes are separated by connective tissue and filled with seminiferous tubules.
        (2) The seminiferous tubules contain undifferentiated cells that give rise to sperm cells.
        (3) The interstitial cells produce male sex hormones.
    b. Formation of sperm cells
        (1) The epithelium lining the seminiferous tubules includes sustentacular cells and spermatogenic cells.
            (a) Sustentacular cells support and nourish spermatogenic cells.
            (b) Spermatogenic cells (spermatogonia) give rise to sperm cells.
        (2) Spermatogenesis produces four sperm cells from each primary spermatocyte.
        (3) Meiosis reduces the number of chromosomes in sperm cells by one-half (from 46 to 23).
    c. Structure of a sperm cell
        A sperm cell consists of a head, midpiece, and tail.
2. Male internal reproductive organs
    a. Epididymides
        (1) Each epididymis is a tightly coiled tube that leads into a ductus deferens.
        (2) They store and nourish immature sperm cells and promote their maturation.
    b. Ductus deferentia
        (1) Each ductus deferens is a muscular tube.
        (2) They pass through the inguinal canal, enter the pelvic cavity, course medially and end behind the urinary bladder.
        (3) They fuse with the ducts from seminal vesicles to form the ejaculatory ducts.
    c. Seminal vesicles
        (1) Each seminal vesicle is a saclike structure attached to a ductus deferens.
        (2) They secrete an alkaline fluid, to help regulate the pH of semen, that contains fructose and prostaglandins.
    d. Prostate gland
        (1) The prostate gland surrounds the urethra just inferior to the urinary bladder.
        (2) It secretes a thin, milky fluid containing citrate and prostate-specific antigen.
    e. Bulbourethral glands
        (1) The bulbourethral glands are two small structures inferior to the prostate gland.
        (2) They secrete a fluid that lubricates the penis in preparation for sexual intercourse.
    f. Semen
        (1) Semen consists of sperm cells and secretions of the seminal vesicles, prostate gland, and bulbourethral glands.
        (2) This fluid is slightly alkaline and contains nutrients and prostaglandins.
        (3) Sperm cells in semen begin to swim, but are unable to fertilize egg cells until they are activated in the female reproductive tract.
3. Male external reproductive organs
    a. Scrotum
        The scrotum is a pouch of skin and subcutaneous tissue that encloses the testes for protection and temperature regulation.
    b. Penis
        (1) The penis becomes erect for insertion into the vagina during sexual intercourse.
        (2) Its body is composed of three columns of erectile tissue.
4. Erection, orgasm, and ejaculation
    a. During erection, vascular spaces in the erectile tissue become engorged with blood.
    b. Orgasm is the culmination of sexual stimulation and is accompanied by emission and ejaculation.
    c. Semen moves along the reproductive tract as smooth muscle in the walls of the tubular structures contracts by reflex.

### 19.3 Hormonal Control of Male Reproductive Functions (p. 526)

1. Hypothalamic and pituitary hormones
    a. The male body remains reproductively immature until the hypothalamus releases gonadotropin-releasing hormone (GnRH), which stimulates the anterior pituitary gland to release gonadotropins.
    b. Follicle-stimulating hormone (FSH) stimulates spermatogenesis.
    c. Luteinizing hormone (LH), sometimes known in males as interstitial cell stimulating hormone (ICSH), stimulates interstitial cells to produce male sex hormones.
2. Male sex hormones
    a. Male sex hormones are called androgens, with testosterone the most important.
    b. Androgen production increases rapidly at puberty.
    c. Actions of testosterone
        (1) Testosterone stimulates development of the male reproductive organs.
        (2) It also develops and maintains male secondary sex characteristics.
    d. Regulation of male sex hormones
        (1) A negative feedback mechanism regulates testosterone concentration.
            (a) A rising testosterone concentration inhibits the hypothalamus and reduces the anterior pituitary gland's secretion of gonadotropins.
            (b) As testosterone concentration falls, the hypothalamus signals the anterior pituitary gland to secrete gonadotropins.
        (2) The testosterone concentration remains relatively stable from day to day.

### 19.4 Organs of the Female Reproductive System (p. 528)

*The primary female sex organs are the ovaries, which produce female sex cells and sex hormones. Accessory sex organs are internal and external.*

1. Ovaries
    a. Ovary structure
        (1) Each ovary is subdivided into a medulla and a cortex.
        (2) The medulla is composed of connective tissue, blood vessels, lymphatic vessels, and nerves.

        - (3) The cortex contains ovarian follicles and is covered by cuboidal epithelium.
    - b. Primordial follicles
        - (1) During prenatal development, groups of cells in the ovarian cortex form millions of primordial follicles.
        - (2) Each primordial follicle contains a primary oocyte and a layer of follicular cells.
        - (3) The primary oocyte begins meiosis, but the process halts until puberty.
        - (4) The number of primary oocytes steadily declines throughout a female's life.
    - c. Oogenesis
        - (1) Beginning at puberty, some primary oocytes are stimulated to continue meiosis.
        - (2) When a primary oocyte undergoes meiosis, it gives rise to a secondary oocyte in which the original chromosome number is reduced by one-half (from 46 to 23).
        - (3) Fertilization of a secondary oocyte produces a zygote.
    - d. Follicle maturation
        - (1) At puberty, FSH initiates follicle maturation.
        - (2) During maturation of the follicle, the follicular cells multiply, and a fluid-filled cavity (antrum) forms.
        - (3) Usually, only one follicle fully develops per reproductive cycle.
        - (4) Just prior to ovulation, the primary oocyte completes meiosis to give rise to a secondary oocyte and first polar body.
    - e. Ovulation
        - (1) Ovulation is the release of a secondary oocyte from an ovary.
        - (2) A rupturing follicle releases the secondary oocyte.
        - (3) After ovulation, the secondary oocyte is drawn into the opening of the uterine tube.
- 2. Female internal reproductive organs
    - a. Uterine tubes
        - (1) The end of each uterine tube expands, and its margin bears irregular extensions.
        - (2) Ciliated cells that line the tube and peristaltic contractions in the wall of the tube help transport the secondary oocyte down the uterine tube. Fertilization of the egg occurs here.
    - b. Uterus
        - (1) The uterus receives the embryo and sustains it during development.
        - (2) The uterine wall includes the endometrium, myometrium, and perimetrium.
    - c. Vagina
        - (1) The vagina receives the erect penis, conveys uterine secretions to the outside, and provides an open channel for the fetus during birth.
        - (2) Its wall consists of mucosal, muscular, and fibrous layers.
- 3. Female external reproductive organs
    - a. Labia majora
        - (1) The labia majora are rounded folds of adipose tissue and skin.
        - (2) The upper ends form a rounded elevation over the pubic symphysis.
    - b. Labia minora
        - (1) The labia minora are flattened, longitudinal folds between the labia majora.
        - (2) They are well supplied with blood vessels.
    - c. Clitoris
        - (1) The clitoris is a small projection at the anterior end of the vulva. It corresponds to the male penis.
        - (2) It is composed of two columns of erectile tissue.
    - d. Vestibule
        - (1) The vestibule is the space between the labia minora.
        - (2) The vestibular glands secrete mucus into the vestibule during sexual stimulation.
- 4. Erection, lubrication, and orgasm
    - a. During periods of sexual stimulation, the erectile tissues of the clitoris and vestibular bulbs become engorged with blood and swell.
    - b. The vestibular glands secrete mucus into the vestibule and vagina.
    - c. During orgasm, the muscles of the perineum, uterine wall, and uterine tubes contract rhythmically.

### 19.5 Hormonal Control of Female Reproductive Functions (p. 534)

*The hypothalamus, anterior pituitary gland, and ovaries secrete hormones that control sex cell maturation, the development and maintenance of female secondary sex characteristics, and changes that occur during the monthly reproductive cycle.*

- 1. Female sex hormones
    - a. A female body remains reproductively immature until about ten years of age, when gonadotropin secretion increases.
    - b. The most important female sex hormones are estrogens and progesterone.
        - (1) Estrogens develop and maintain most of the female secondary sex characteristics.
        - (2) Progesterone prepares the uterus for pregnancy.
- 2. Female reproductive cycle
    - a. FSH from the anterior pituitary gland initiates a reproductive cycle by stimulating follicle maturation.
    - b. Maturing follicular cells secrete estrogens, which maintain the secondary sex characteristics and thicken the uterine lining.
    - c. Secretion of a relatively large amount of LH (LH "surge") by the anterior pituitary gland leads to ovulation. The LH surge causes the primary oocyte to complete meiosis, giving rise to a secondary oocyte and first polar body.
    - d. Following ovulation, follicular cells give rise to the corpus luteum.
        - (1) The corpus luteum secretes estrogens and progesterone, which causes the endometrium to become more vascular and glandular.
        - (2) If a secondary oocyte is not fertilized, the corpus luteum begins to degenerate.
        - (3) As concentrations of estrogens and progesterone decline, the uterine lining disintegrates, causing menstrual flow.
    - e. During this cycle, estrogens and progesterone inhibit the release of LH and FSH (except for the large increase at mid-cycle). As concentrations of estrogens and progesterone decline, the anterior pituitary gland secretes FSH and LH again, stimulating a new reproductive cycle.
- 3. Menopause
    - a. Menopause is termination of reproductive cycles due to production of lesser amounts of estrogen and progesterone.
    - b. Reduced concentrations of estrogens and lack of progesterone may cause regressive changes in female secondary sex characteristics.

### 19.6 Mammary Glands (p. 538)

1. The mammary glands are in the subcutaneous tissue of the anterior thorax within the breasts.
2. They are composed of lobes that contain glands and ducts.
3. Dense connective and adipose tissues separate the lobes.
4. Ducts connect the mammary glands to the nipple.

5. Ovarian hormones stimulate female breast development.
   a. Alveolar glands and ducts enlarge.
   b. Fat is deposited around and within the breasts.

### 19.7 Birth Control (p. 538)

*Birth control is voluntary regulation of how many offspring are produced and when they are conceived. It usually involves some method of contraception.*

1. Coitus interruptus is withdrawal of the penis from the vagina before ejaculation.
2. The rhythm method is abstinence from sexual intercourse for several days before and after ovulation.
3. Mechanical barriers
   a. Males and females can use condoms.
   b. Females can also use diaphragms, cervical caps, and cervical shields.
4. Chemical barriers
   Spermicidal creams, foams, and jellies provide an unfavorable environment in the vagina for sperm survival.
5. Combined hormone contraceptives
   a. A flexible ring inserted deep into the vagina, a plastic patch, or a pill can deliver estrogen and progestin to prevent pregnancy.
   b. They disrupt a female's normal pattern of gonadotropin secretion, which prevents follicle maturation and ovulation, and they thicken cervical mucus to prevent the sperm from joining the egg.
6. Other hormone contraceptives
   a. Intramuscular injection with medroxyprogesterone every three months acts similarly to oral contraceptives to prevent pregnancy.
   b. An implantable rod containing progestin may prevent pregnancy for up to three years.
7. Intrauterine devices (IUDs)
   An IUD is a solid object inserted in the uterine cavity that prevents pregnancy by interfering with implantation of a blastocyst.
8. Sterilization
   a. Vasectomies in males and tubal ligations in females are surgical sterilization procedures.
   b. A nonsurgical method involves insertion of a tiny coil into each uterine tube, causing scarring that blocks the sperm from joining the egg.

### 19.8 Sexually Transmitted Infections (p. 543)

1. Sexually transmitted infections are passed during sexual contact and may go undetected for years.
2. Many of the diseases associated with sexually transmitted infections share similar symptoms.

## CHAPTER ASSESSMENTS

### 19.1 Introduction

**1.** General functions of the male and female reproductive systems include ____________________________. (p. 519)
   a. producing sex cells
   b. transporting sex cells to sites of fertilization
   c. secreting hormones
   d. all of the above

### 19.2 Organs of the Male Reproductive System

**2.** List the organs (both primary and accessory) of the male reproductive system, and explain how each organ's structure affects the organ's function. (pp. 519–525)
**3.** List the major steps in spermatogenesis. (pp. 520–521)
**4.** Trace the path of sperm cells from their site of formation to the outside. Indicate composition and when and where secretions are added to produce semen. (pp. 520–525)
**5.** Distinguish between emission and ejaculation. (p. 525)

### 19.3 Hormonal Control of Male Reproductive Functions

**6.** Describe the role of gonadotropin-releasing hormone (GnRH) in the control of male reproductive functions. (p. 526)
**7.** Discuss the actions of testosterone. (pp. 526–528)

### 19.4 Organs of the Female Reproductive System

**8.** List the organs (both primary and accessory) of the female reproductive system, and explain how each organ's structure affects the organ's function. (pp. 528–534)
**9.** List the major steps in oogenesis. (p. 529)
**10.** Describe how a follicle matures. (pp. 530–531)
**11.** Define *ovulation.* (p. 531)

### 19.5 Hormonal Control of Female Reproductive Functions

**12.** Describe the role of gonadotropin-releasing hormone (GnRH) in the control of female reproductive functions. (p. 534)
**13.** Discuss the actions of estrogens. (pp. 534–535)
**14.** Summarize the major events in the reproductive cycle. (pp. 535–536)

### 19.6 Mammary Glands

**15.** Describe the structure of a mammary gland. (p. 538)

### 19.7 Birth Control

**16.** Match the birth control method with its description. (pp. 539–542)

(1) withdrawal
(2) rhythm method
(3) condom
(4) spermicide (foam, gel)
(5) estrogen/progesterone
(6) IUD
(7) vasectomy
(8) tubal ligation

A. kills sperm (not very effective when used alone)
B. keeps sperm out of vagina or from entering cervix (additionally, may help prevent disease)
C. prevents implantation of blastocyst
D. no intercourse during fertile times (ineffective)
E. penis removed from vagina before ejaculation
F. sperm cells never reach penis (very effective)
G. prevents follicle maturation and ovulation
H. oocytes never reach uterus (very effective)

### 19.8 Sexually Transmitted Infections

**17.** Common symptoms of diseases associated with sexually transmitted infections include ____________________________. (p. 543)
   a. a burning sensation during urination
   b. discharge from vagina or penis
   c. sores, blisters, or rash on genitals
   d. all of the above

**18.** If left untreated, a complication of the diseases gonorrhea and chlamydia is _____________. (p. 543)

## INTEGRATED ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 11.5, 11.8, 19.2, 19.3, 19.4, 19.5, 19.7

1. Understanding the causes of infertility can be valuable in developing new birth control methods. Cite a type of contraceptive based on each of the following causes of infertility:
   (a) failure to ovulate due to a hormonal imbalance;
   (b) a large fibroid tumor that disturbs the uterine lining;
   (c) endometrial tissue blocking uterine tubes;
   (d) low sperm count (too few sperm per ejaculate).

### OUTCOMES 11.5, 11.8, 19.2, 19.4

2. What changes, if any, would a male who has had one testis removed experience? A female who has had one ovary removed?

### OUTCOME 19.2, 19.4

3. Some men are unable to become fathers because their spermatids do not mature into sperm. Injection of their spermatids into their partners' secondary oocytes sometimes results in conception. A few men have fathered healthy babies this way. Why would this procedure work with spermatids, but not with primary spermatocytes?

### OUTCOME 19.4

4. Sometimes a sperm cell fertilizes a polar body rather than a secondary oocyte. An embryo does not develop, and the fertilized polar body degenerates. Why is a polar body unable to support development of an embryo?

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# 20

# Pregnancy, Growth, Development, and Genetics

*Widespread use of sperm from a single donor can create dozens of donor half-siblings.*

Sperm donation can create many donor half-siblings. Before the age of the Internet, it was highly unusual for children conceived with the same donated sperm to meet each other. Today half-siblings can find each other and are even meeting, thanks to the Donor Sibling Registry. This and other websites enable parents who used donated sperm to learn of other families that used the same sperm, using identifying numbers that the sperm banks assigned. Several of these half-sibling groups number up to 50, with one including 150 children who share their father, but not their mothers.

Some families who discover many half-siblings react positively, even holding social events where everyone marvels at the resemblances among the children. But others seek legislation limiting the number of children a single sperm donor can father. Because mothers are not required to report births using sperm donors to the facilities that provided the sperm, the true number of children born each year using donor sperm is unknown.

Use of sperm from one donor to inseminate many women can have negative biological consequences. Two half-siblings might wish to start a family, not knowing they are related. Overrepresentation of one individual's contribution to the next generation can affect the gene pool, increasing the prevalence of mutations that cause rare inherited diseases, because a man would not ordinarily father 50 to 100 children.

Many people who find out that their children have dozens of half-siblings are upset, as are the men who donate the sperm. The American Society for Reproductive Medicine advises that one man's donated sperm be used for no more than 25 births for every 800,000 births, but these recommendations are not enforced, although similar guidelines are in several European nations.

## LEARNING OUTCOMES

*After studying this chapter, you should be able to do the following:*

**20.1 Introduction**

1. Distinguish between growth and development. (p. 550)
2. Distinguish between prenatal and postnatal. (p. 550)

**20.2 Fertilization**

3. Describe fertilization. (p. 550)

**20.3 Pregnancy and the Prenatal Period**

4. List and provide details of the major events of cleavage. (p. 552)
5. Distinguish between an embryo and a fetus. (p. 553)
6. Discuss the hormonal changes in the maternal body during pregnancy. (p. 556)
7. Describe the major events of the embryonic stage of development. (pp. 556–560)
8. List the structures produced by each of the primary germ layers. (p. 557)
9. Describe the major events of the fetal stage of development. (pp. 560–561)
10. Trace the path of blood through the fetal cardiovascular system. (pp. 561–563)
11. Explain the role of hormones in the birth process and milk production. (pp. 564–566)

Anatomy & Physiology REVEALED aprevealed.com **Module 14** Reproductive System

**20.4 Postnatal Period**

**12.** Describe the major cardiovascular and other physiological adjustments in the newborn. (pp. 566–567)

**20.5 Aging**

**13.** Distinguish between passive aging and active aging. (pp. 567 and 569)

**20.6 Genetics**

**14.** Distinguish among the modes of inheritance. (pp. 571–572)

**15.** Describe the components of multifactorial traits. (pp. 573–574)

## AIDS TO UNDERSTANDING WORDS *(Appendix A on page 577 has a complete list of Aids to Understanding Words.)*

**allant-** [sausage] *allant*ois: Tubelike structure extending from the yolk sac into the connecting stalk of an embryo.

**chorio-** [skin] *chorio*n: Outermost membrane surrounding the fetus and its membranes.

**cleav-** [to divide] *cleav*age: Period of development when a zygote divides, producing increasingly smaller cells.

**hetero-** [other, different] *hetero*zygous: When the two copies of a gene variant in an individual are of different DNA sequence.

**hom-** [same, common] *hom*ozygous: When the two copies of a gene variant in an individual are identical in DNA sequence.

**lacun-** [pool] *lacun*a: Space between the chorionic villi that fills with maternal blood.

**morul-** [mulberry] *morul*a: Embryonic structure consisting of a solid ball of about sixteen cells that resembles a mulberry.

**nat-** [to be born] pre*nat*al: Before birth.

**troph-** [well fed] *troph*oblast: Cellular layer that surrounds the inner cell mass and helps nourish it.

**umbil-** [navel] *umbil*ical cord: Structure attached to the fetal navel (umbilicus) that connects the fetus to the placenta.

---

## 20.1 | Introduction

A sperm cell and an egg cell (secondary oocyte) unite, forming a zygote, and the journey of prenatal development begins. Following thirty-eight weeks of cell division, growth, and specialization into distinctive tissues and organs, a new human being enters the world.

Humans grow, develop, and age. **Growth** is an increase in size. In humans and other many-celled organisms, growth entails an increase in cell numbers as a result of mitosis, followed by enlargement of the newly formed cells.

**Development,** which includes growth, is the continuous process by which an individual changes from one life phase to another. These life phases include a **prenatal period** (pre-na′tal pe′re-od), which begins with fertilization and ends at birth, and a **postnatal** (pōst-na′tal) **period,** which begins at birth and ends with death.

### PRACTICE

1. Describe growth of an individual.
2. When is the beginning and ending of the postnatal period?

---

## 20.2 | Fertilization

The union of a secondary oocyte and a sperm cell is called **fertilization** (fer″tĭ-lĭ-za′shun), or conception. Fertilization takes place in a uterine tube.

### Transport of Sex Cells

Each month, a female of reproductive age usually ovulates a secondary oocyte, unless she is anovulatory, as discussed in Clinical Application 20.1. The released egg cell then usually enters a uterine tube. During sexual intercourse, the male deposits semen containing sperm cells in the vagina near the cervix. To reach the secondary oocyte, the sperm cells must then move upward through the uterus and uterine tube. Prostaglandins in the semen stimulate lashing of sperm tails, and muscular contractions within the walls of the uterus and uterine tube aid the sperm cells' journey. Also, under the influence of high concentrations of estrogens during the first part of the reproductive cycle, the uterus and cervix secrete a watery fluid that promotes sperm transport and survival. Conversely, during the latter part of the cycle, when the progesterone concentration is high, the female reproductive tract secretes a viscous fluid that hampers sperm transport and survival. Sperm cells reach the upper part of the uterine tube in less than an hour following sexual intercourse. Many sperm cells may reach a secondary oocyte, but usually only one sperm cell fertilizes it (fig. 20.1; see fig. 20.4*a*).

Two definitions can be found for the term "embryo." A usage encountered commonly in recent years indicates that the embryo begins with fertilization of the egg and lasts for approximately eight weeks, at which point the embryo becomes a fetus. The definition more consistent with development, and used in this textbook, considers an embryo to exist when the primary germ layers have formed, two weeks after fertilization, continuing through week eight. Prior to that is the pre-embryo.

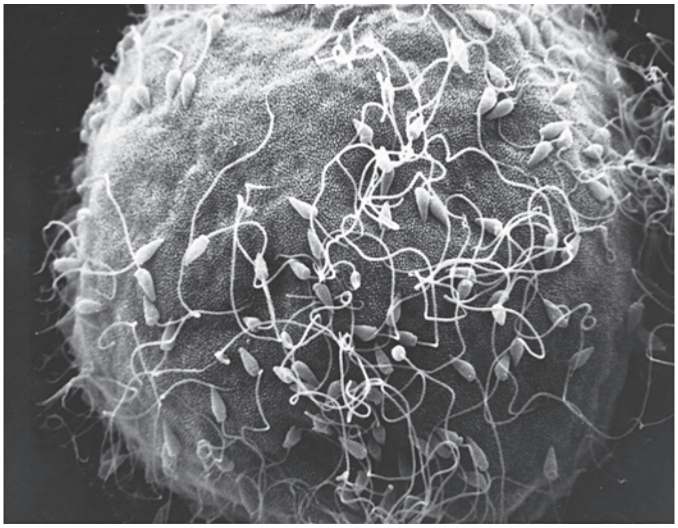


**FIGURE 20.1** Scanning electron micrograph of sperm cells on the surface of a secondary oocyte (1,100×). Only one sperm cell actually fertilizes a secondary oocyte.

## Sperm Cell Joins Egg Cell

A sperm cell first invades the corona radiata, the layers of follicular cells that adhere to the secondary oocyte's surface, then binds to the *zona pellucida,* a membrane rich in glycoproteins that surrounds the secondary oocyte's cell membrane. An enzyme associated with the sperm cell membrane (hyaluronidase) aids penetration of the sperm head by digesting proteins in the corona radiata (fig. 20.2). Once through the corona radiata, sperm must next penetrate the zona pellucida, the layer closest to the oocyte membrane. As sperm bind to a specific class of protein on the zona pellucida, the acrosomes release their enzymes by exocytosis, and those enzymes digest the material of the zona pellucida.

Hundreds of sperm take part in removing these barriers, but only one sperm, the first to reach the oocyte membrane, will actually fertilize the oocyte. The head portion of that first sperm cell fuses with the oocyte membrane, and the sperm nucleus enters the oocyte, leaving the mitochondria-rich middle section and tail outside. Sperm entry triggers lysosome-like vesicles just beneath the oocyte cell membrane to release enzymes that harden the zona pellucida. This reduces the chance that other sperm cells will penetrate. The sperm cell nucleus enters the secondary oocyte's cytoplasm and swells. The secondary oocyte then divides unequally to form a large cell, whose nucleus contains the female's genetic contribution, and a tiny second polar body, which is later expelled. Meiosis is completed. The approaching nuclei from the two sex cells are called pronuclei, until they meet and merge (fig. 20.3). When the pronuclei unite, their nuclear membranes disassemble, and their chromosomes mingle, completing fertilization. This cell, called a **zygote** (zi′gōt), is the first cell of the future offspring.

Each sex cell provides 23 chromosomes, so the product of fertilization is a cell with 46 chromosomes—the usual number in a human body cell (somatic cell). Table 20.1 describes assisted reproductive technologies used to achieve fertilization.

### PRACTICE

3. What factors aid the movements of the secondary oocyte and sperm cells through the female reproductive tract?
4. Where in the female reproductive system does fertilization take place?
5. List the events of fertilization.

## 20.3 | Pregnancy and the Prenatal Period

**Pregnancy** (preg′nan-se) is the presence of a developing offspring in the uterus. Pregnancy consists of three periods called trimesters, each about three months long.

The prenatal period of development of the offspring usually lasts for thirty-eight weeks from conception. It can be divided into a period of cleavage, an embryonic stage, and a fetal stage.

### CAREER CORNER
### Genetic Counselor

The pregnant patient is anxious following the phone call reporting the test result that she is a carrier for cystic fibrosis. She soon meets with a genetic counselor, who explains how the disease is inherited. The next step is to test the father, and when he is found not to have a mutation, the couple relaxes. Had he also carried a mutation, the counselor explained, the child and any future children would have 25% chance of inheriting the disease, which further testing could detect.

A genetic counselor is trained in genetics, psychology, and counseling techniques to provide guidance to patients taking genetic tests or with inherited diseases in their families. A certified genetic counselor has a master's degree in the field, but nurses, social workers, physicians, and PhD geneticists can also provide genetic counseling. The counselor explains the inheritance pattern, assesses risks for specific individuals in a family, recommends tests, and interprets the results.

Genetic counselors work in medical centers, in physicians' offices, and at companies that provide genetic tests. They may specialize in prenatal care or work in clinics for patients with specific diseases.

## CLINICAL APPLICATION 20.1

## Female Infertility

*Infertility* is the inability to conceive after a year of trying. In 90% of cases, infertility has a physical cause, and 60% of the time the abnormality is in the female's reproductive system. A common cause of female infertility is insufficient secretion (hyposecretion) of gonadotropic hormones by the anterior pituitary, preventing ovulation (anovulation). Testing the urine for *pregnanediol,* a product of progesterone metabolism, can detect an anovulatory ovarian cycle. Because progesterone concentration normally rises following ovulation, no increase in pregnanediol in the urine during the latter part of the ovarian cycle suggests lack of ovulation.

Fertility specialists can treat anovulation due to hyposecretion of gonadotropic hormones by administering human chorionic gonadotropin (hCG) obtained from human placentas. Another ovulation-stimulating biochemical, human menopausal gonadotropin (hMG), contains luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and is obtained from the urine of postmenopausal women. However, either hCG or hMG may overstimulate the ovaries and cause many follicles to release secondary oocytes simultaneously, which may result in multiple births.

Another cause of female infertility is *endometriosis,* in which small pieces of the uterine lining (endometrium) move up through the uterine tubes during menstruation and attach somewhere in the abdominal cavity. Here the tissue changes as it would in the uterine lining during the ovarian cycle. The misplaced tissue breaks down at the end of the cycle but cannot be expelled. Instead it remains in the abdominal cavity, irritating the lining (peritoneum) and causing considerable pain. This tissue also stimulates formation of fibrous tissue (fibrosis), which may encase the ovary and prevent ovulation or obstruct the uterine tubes. Conception may become impossible.

Sexually transmitted infections (STIs), such as gonorrhea, can cause female infertility. These infections can inflame and obstruct the uterine tubes or stimulate production of viscous mucus that can plug the cervix and prevent sperm entry.

Women become infertile if their ovaries are removed, which may be part of cancer treatment, or are damaged by cancer treatment. To make future pregnancies possible, these women can have strips of ovarian tissue removed before their cancer treatment begins. The strips are frozen and stored, then thawed and reimplanted under the skin of the forearm or abdomen or in the pelvic cavity near the ovaries. Secondary oocytes are collected and fertilized *in vitro.* Egg freezing is no longer considered experimental, but it is more successful for the eggs of younger women.

Finding the right treatment for a particular patient requires determining the infertility's cause. Table 20A describes diagnostic tests for female infertility.

**Table 20A** **Tests to Assess Female Infertility**

| Test | What It Checks |
|---|---|
| Hormone levels | If ovulation occurs |
| Ultrasound | Placement and appearance of reproductive organs and structures |
| Postcoital test | Cervix examined soon after unprotected intercourse to see if mucus is thin enough to allow sperm through |
| Endometrial biopsy | Small piece of uterine lining sampled and viewed under microscope to see if it can support an embryo |
| Hysterosalpingogram | Dye injected into uterine tube and followed with scanner shows if tube is clear or blocked |
| Laparoscopy | Small, lit optical device inserted near navel to detect scar tissue blocking tubes, which ultrasound may miss |

## Period of Cleavage

About thirty hours after the zygote forms, it undergoes *mitosis,* giving rise to two new cells (blastomeres) (fig. 20.4*b*). These cells, in turn, divide into four cells, which divide into eight cells, and so forth. The divisions occur rapidly, with little time for the cells to grow. As a result, each division yields smaller cells. This phase of early rapid cell division is termed **cleavage** (klēv′ij) (see fig. 20.3).

During cleavage, the tiny mass of cells moves through the uterine tube to the uterine cavity. The trip takes about three days, and by then the structure consists of a solid ball, called a *morula* (mor′u-lah), of about sixteen cells (figs. 20.3 and 20.4*c*).

The morula remains free within the uterine cavity for about three days. During this stage, the zona pellucida of the original secondary oocyte degenerates. Then the morula hollows out, forming a *blastocyst,* which begins to attach to the endometrium. By the end of the first week of development, the blastocyst superficially implants in the endometrium (fig. 20.5). Up until this point, the cells that will become the developing off-

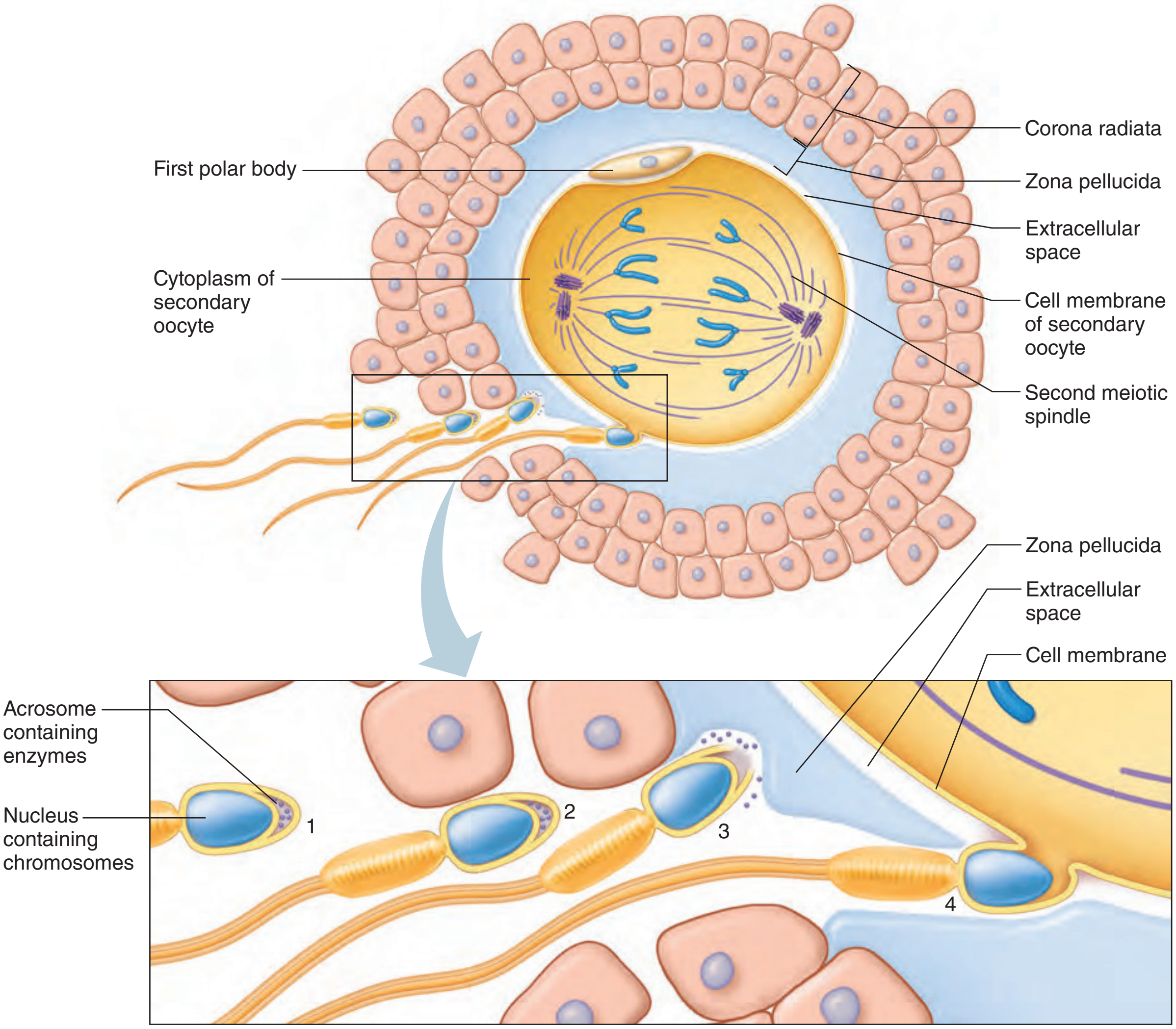

First polar body
Cytoplasm of secondary oocyte
Corona radiata
Zona pellucida
Extracellular space
Cell membrane of secondary oocyte
Second meiotic spindle
Zona pellucida
Extracellular space
Cell membrane
Acrosome containing enzymes
Nucleus containing chromosomes
1
2
3
4

**FIGURE 20.2** Steps in fertilization: (**1**) The sperm cell reaches the corona radiata surrounding the secondary oocyte. (**2**) An enzyme on the sperm surface digests a path through the corona radiata. (**3**) The sperm binds to proteins in the zona pellucida, triggering the release of digestive enzymes from the acrosome by exocytosis. (**4**) Once the sperm is through the zona pellucida, the sperm head fuses with the oocyte membrane, and the sperm nucleus enters the oocyte. Although only a single sperm can fertilize the egg, hundreds of sperm are necessary to break down these barriers encountered along the way.

Q *How many chromosomes are contained in the secondary oocyte prior to fertilization?*

**Answer can be found in Appendix F on page 582.**

spring are pluripotent stem cells (see fig. 20.3), which means they can give rise to several specialized types of cells, as well as yield additional stem cells.

An ectopic pregnancy occurs when the very early embryo implants outside the uterus, such as in a uterine tube, on an ovary, on the cervix, or on an organ in the abdominal cavity. A fertilized egg implanting in a uterine tube is a *tubal pregnancy,* a form of ectopic pregnancy. The tube usually ruptures as the embryo enlarges, resulting in severe pain and heavy vaginal bleeding. Treatment is prompt surgical removal of the embryo and repair or removal of the damaged uterine tube.

At about the time of implantation, certain cells on the inner face of the blastocyst organize into a group, called the inner cell mass, that will give rise to the body of the developing offspring. This marks the beginning of the **embryonic stage** of development. The offspring is termed an **embryo** (em′bre-o) until the end of the eighth week, when the basic structural form of the human body is recognizable. After the eighth week and until birth, the offspring is called a **fetus** (fe′tus). Rudiments of all organs are present by the end of embryonic development. These organs and other structures enlarge and specialize during fetal development.

During the embryonic stage, the cells surrounding the embryo, with cells of the endometrium, form a

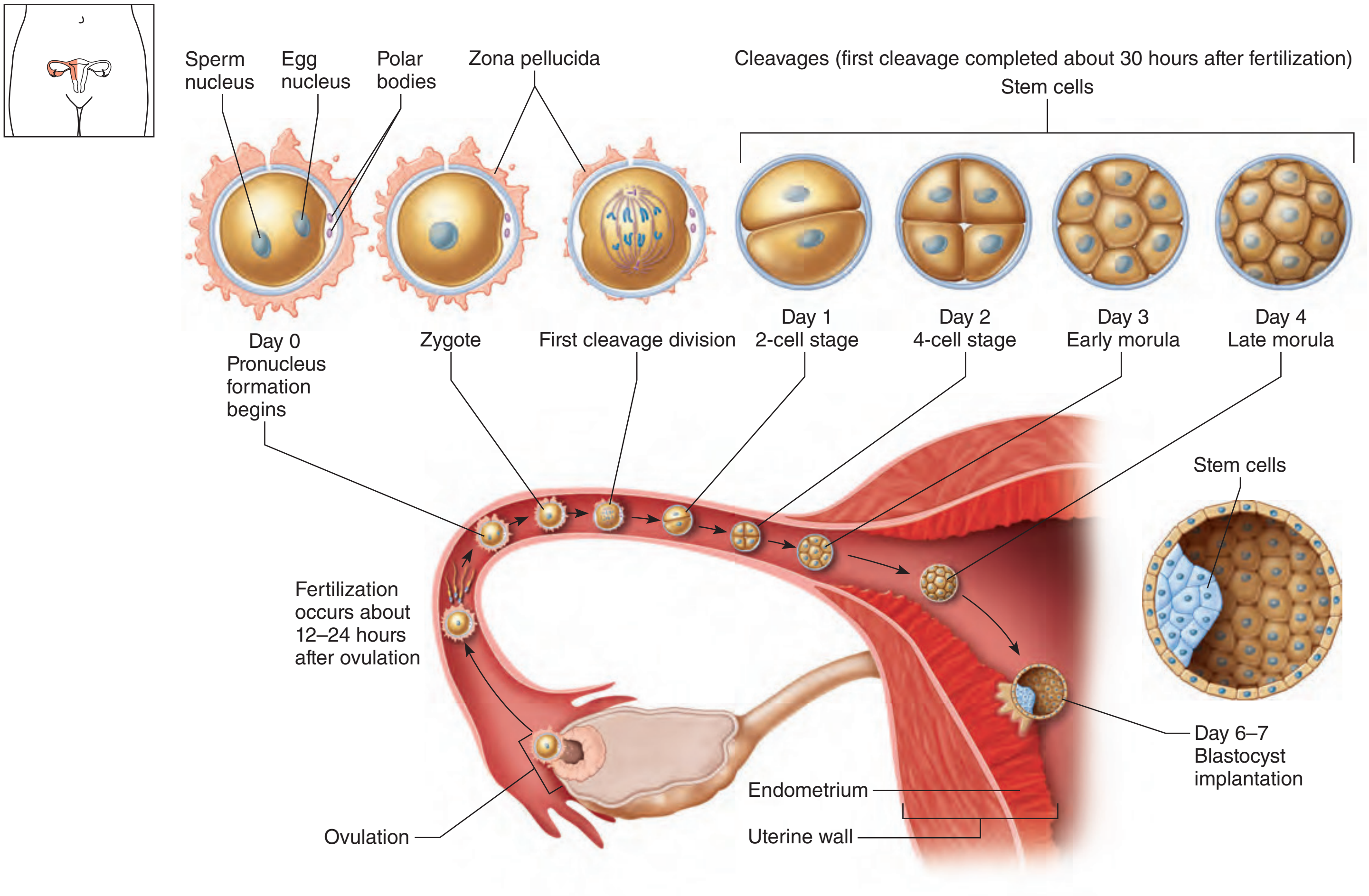

Sperm nucleus
Egg nucleus
Polar bodies
Zona pellucida
Cleavages (first cleavage completed about 30 hours after fertilization)
Stem cells
Day 0
Pronucleus formation begins
Zygote
First cleavage division
Day 1
2-cell stage
Day 2
4-cell stage
Day 3
Early morula
Day 4
Late morula
Stem cells
Fertilization occurs about 12–24 hours after ovulation
Day 6–7
Blastocyst implantation
Endometrium
Uterine wall
Ovulation

**FIGURE 20.3** APR Stages of early human prenatal development.

## Table 20.1 Assisted Reproductive Technologies

| Technology | Condition It Treats | Procedure |
|---|---|---|
| Intrauterine insemination | Male infertility—lack of sperm cells or low sperm count | Donated sperm cells are placed into the cervix or uterus. |
| Surrogate mother | Female infertility—a woman has healthy ovaries, but lacks a uterus | A secondary oocyte fertilized *in vitro* is implanted in a woman other than its donor. The surrogate, or "gestational mother," gives the newborn to the "genetic mother" and her partner, the sperm donor. |
| Gamete intrafallopian transfer (GIFT) | Female infertility—bypasses blocked uterine tube | Secondary oocytes are removed from a woman's ovary, then placed along with donated sperm cells into a uterine tube at a site past any obstruction. |
| Zygote intrafallopian transfer (ZIFT) | Female infertility—bypasses blocked uterine tube | A secondary oocyte fertilized *in vitro* is placed in a uterine tube past the blockage. It travels to the uterus on its own. |
| Embryo adoption | Female infertility—a woman has nonfunctional ovaries, but a healthy uterus | A woman is artificially inseminated with sperm cells from a man whose partner cannot ovulate. If the woman conceives, the morula is flushed from her uterus and implanted in the uterus of the sperm donor's partner. |
| Intracytoplasmic sperm injection | Low sperm count; sperm that cannot mature past spermatid stage; men with paralysis who cannot ejaculate | Sperm or spermatids are injected into secondary oocytes *in vitro*. |

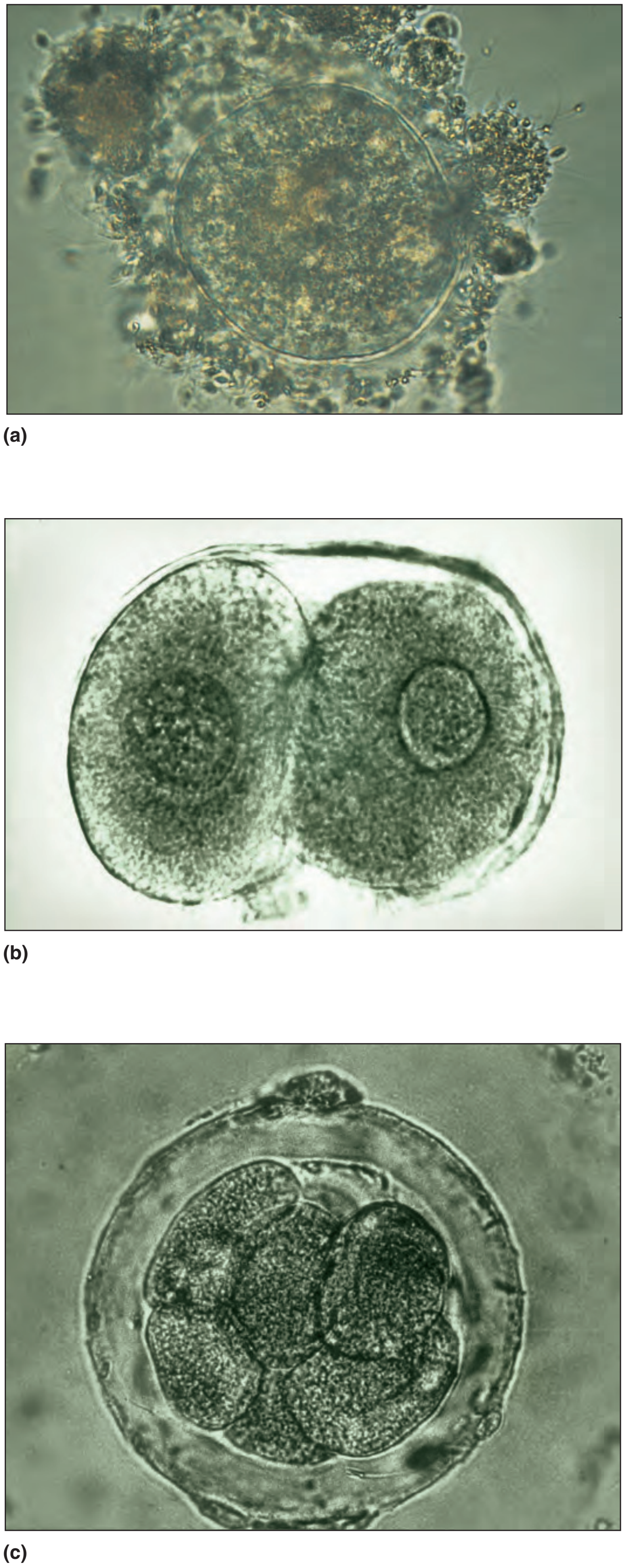


**FIGURE 20.4** Light micrographs of (**a**) a human secondary oocyte surrounded by follicular cells and sperm cells (250×), (**b**) the two-cell stage (600×), and (**c**) a morula (500×).

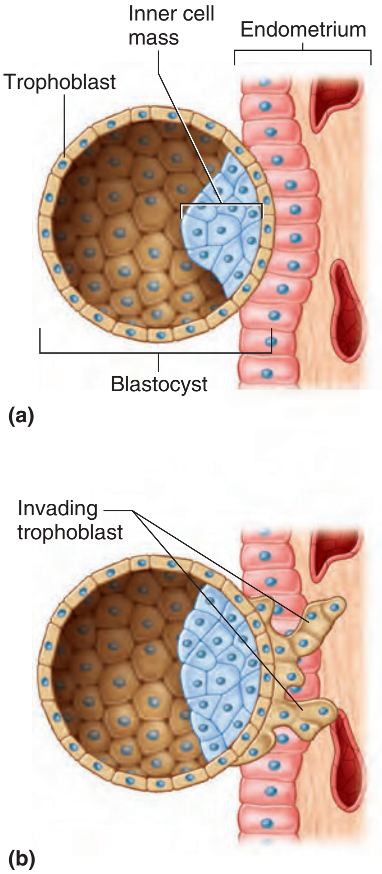


**FIGURE 20.5** APR About the sixth day of prenatal development, the blastocyst (**a**) contacts the uterine wall and (**b**) begins to implant. The trophoblast, which will help form the placenta, secretes hCG, a hormone that maintains the pregnancy.

complex vascular structure called the **placenta** (plah-sen′tah). This organ anchors the embryo to the uterine wall and exchanges nutrients, gases, and wastes between maternal blood and the embryo's blood. The placenta also secretes hormones.

Fraternal (dizygotic) twins develop if two ovarian follicles release secondary oocytes simultaneously and both are fertilized. Such twins are no more alike genetically than any nontwin siblings.

Identical (monozygotic) twins develop from a single fertilized secondary oocyte if two inner cell masses form within a blastocyst and each produces an embryo. Twins of this type usually share a single placenta, and they are genetically identical. Therefore, they are always the same sex and are similar in appearance.

## PRACTICE

6. What is cleavage?
7. What is implantation?
8. How do an embryo and a fetus differ?

## Hormonal Changes During Pregnancy

During a typical reproductive cycle, the corpus luteum degenerates about two weeks after ovulation. Consequently, concentrations of estrogens and progesterone decline rapidly, the uterine lining breaks down, and the endometrium sloughs away as menstrual flow. If this occurs following implantation, the embryo is lost in a spontaneous abortion.

The hormone **human chorionic gonadotropin (hCG)** normally prevents spontaneous abortion. It is secreted by cells from the outer blastocyst that form a layer called the trophoblast, which surrounds the developing embryo and later helps form the placenta (fig. 20.5). This hormone, similar in function to luteinizing hormone (LH), maintains the corpus luteum, which continues secreting estrogens and progesterone, stimulating the uterine wall to grow and develop. At the same time, hCG inhibits the anterior pituitary gland's release of follicle-stimulating hormone (FSH) and LH, halting the normal reproductive cycle.

Secretion of hCG continues at a high level for about two months and then declines by the end of four months. Detecting this hormone in urine or blood is the basis of pregnancy tests. The corpus luteum persists throughout pregnancy, but its function as a hormone source becomes less important after the first three months (first trimester), when the placenta secretes sufficient estrogens and progesterone (fig. 20.6).

For the remainder of the pregnancy, *placental estrogens* and *placental progesterone* maintain the uterine wall. The placenta also secretes a hormone called **placental lactogen** that, with placental estrogens and progesterone, stimulates breast development and prepares the mammary glands to secrete milk. Placental progesterone and a polypeptide hormone called *relaxin* from the corpus luteum inhibit the smooth muscle in the myometrium, suppressing uterine contractions until the birth process begins.

The high concentration of placental estrogens during pregnancy enlarges the vagina and external reproductive organs. Also, relaxin relaxes the connective tissue of the pubic symphysis and sacroiliac joints during the last week of pregnancy, allowing greater movement at these joints and aiding the passage of the fetus through the birth canal.

Other hormonal changes of pregnancy include increased adrenal secretion of aldosterone, which promotes renal reabsorption of sodium and leads to fluid retention. The parathyroid glands secrete parathyroid hormone, which helps maintain a high concentration of maternal blood calcium (see chapter 11, pp. 312–313). Table 20.2 summarizes the hormonal changes of pregnancy.

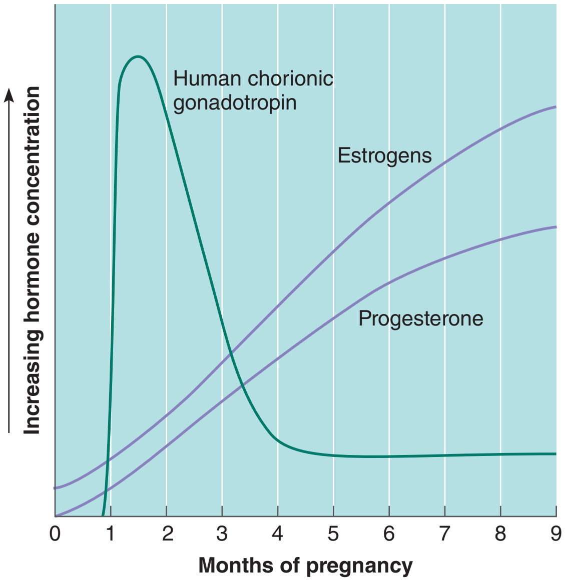


**FIGURE 20.6** The relative concentrations of three hormones in maternal blood change during pregnancy.

**PRACTICE**

9. Which hormone normally prevents spontaneous abortion?
10. What are the sources of the hormones that sustain the uterine wall during pregnancy?
11. What other hormonal changes occur during pregnancy?

Very early in pregnancy, while vast hormonal changes sweep a woman's body and the embryo rapidly increases in size and complexity, the woman may not yet realize she is pregnant. Early signs of pregnancy resemble those of approaching menstruation, such as bloating. As the pregnancy continues, the woman's blood volume increases by one-third, and her bones may weaken if she does not receive adequate dietary calcium. Muscle spasms may occur in response to electrolyte imbalances. In the later months, the enlarging uterus pushing against the woman's abdominopelvic organs can produce heartburn, shortness of breath, and an increased urge to urinate. Fetal movements become noticeable by the fourth or fifth month, first as slight flutterings, then as jabs, kicks, and squirming movements.

## Embryonic Stage

The embryonic stage extends from the beginning of the second week through the eighth week of prenatal development. During this time the placenta forms, the main internal organs develop, and the major external body structures appear.

As the embryo implants in the uterus, proteolytic enzymes from the trophoblast break down endometrial tissue, providing nutrients for the developing embryo. A second layer of cells begins to line the trophoblast, and together those two layers form a structure called the **chorion** (ko′re-on). Soon slender projections, including the new cell layer, grow out from the trophoblast, making their way into the surrounding endometrium by erod-

## TABLE 20.2 Hormonal Changes During Pregnancy

1. Following implantation, cells of the trophoblast begin to secrete human chorionic gonadotropin (hGC).
2. Human chorionic gonadotropin maintains the corpus luteum, which continues to secrete estrogens and progesterone.
3. As the placenta develops it secretes abundant estrogens and progesterone.
4. Placental estrogens and progesterone:
    a. stimulate the uterine lining to continue development.
    b. maintain the uterine lining.
    c. inhibit secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary gland.
    d. stimulate development of mammary glands.
    e. inhibit uterine contractions (progesterone).
    f. enlarge the reproductive organs (estrogens).
5. Relaxin from the corpus luteum also inhibits uterine contractions and relaxes the pelvic ligaments.
6. The placenta secretes placental lactogen that stimulates breast development.
7. Aldosterone from the adrenal cortex promotes renal reabsorption of sodium.
8. Parathyroid hormone from the parathyroid glands helps maintain a high concentration of maternal blood calcium.

ing it with their secretions of proteolytic enzymes. These projections become increasingly complex and form the highly branched **chorionic villi**, which are well established by the end of the fourth week (fig. 20.7).

Continued secretion of proteolytic enzymes forms irregular spaces called **lacunae** in the endometrium around and between the chorionic villi. These spaces fill with maternal blood that escapes from endometrial blood vessels eroded by enzyme action. At the same time, embryonic blood vessels extend through the *connecting stalk*, which attaches the embryo to the developing placenta. They establish capillary networks in the developing chorionic villi. These embryonic vessels allow nutrient exchange with the blood in the lacunae, meeting the increased nutrient demands of the growing embryo.

While the placenta is forming from the chorion, a second membrane, called the **amnion** (am′ne-on), develops around the embryo (fig. 20.8). It appears during the second week. Its margin is attached around the edge of the embryonic disc, and fluid called **amniotic fluid** fills the space between the amnion and the embryonic disc. The amniotic fluid allows the embryo to grow freely without compression from surrounding tissues, protects the embryo from jarring movements of the woman's body, and helps to maintain a stable temperature for embryonic and fetal development.

By the end of the second week, the inner cell mass has flattened into an **embryonic disc** with two distinct layers—an outer *ectoderm* and an inner *endoderm*. A short time later the ectoderm and endoderm fold, and a third layer of cells, the *mesoderm*, forms between them. All organs form from these three cell layers, called the **primary germ layers** (pri′mar-e jerm la′erz) (fig. 20.7). The two-week embryo, with its three primary germ layers, is called a **gastrula** (gas′troo-lah). Table 20.3 summarizes the stages of early human prenatal development.

Ectodermal cells give rise to the nervous system, parts of special sensory organs, the epidermis, hair, nails, glands of the skin, and linings of the mouth and anal canal. Mesodermal cells form all types of muscle tissue, bone tissue, bone marrow, blood, blood vessels, lymphatic vessels, internal reproductive organs, kidneys, and the epithelial linings of the body cavities. Endodermal cells produce the epithelial linings of the digestive tract, respiratory tract, urinary bladder, and urethra.

## PRACTICE

12. Describe the structure of a chorionic villus.
13. What is the function of the amniotic fluid?
14. Which tissues and structures develop from ectoderm? From mesoderm? From endoderm?

In addition to the chorion and amnion, two other extra-embryonic membranes form during development—the yolk sac and the allantois (fig. 20.8). ("Extra-embryonic" refers to structures that are distinct from the embryo.) The **yolk sac** forms during the second week and is attached to the underside of the embryonic disc. It forms blood cells in the early stages of development and gives rise to the cells that later become sex cells. The **allantois** (ah-lan′to-is) forms during the third

## TABLE 20.3 Stages and Events of Early Human Prenatal Development

| Stage | Time Period | Principal Events |
|---|---|---|
| Zygote | 12–24 hours following ovulation | Secondary oocyte is fertilized, meiosis is completed; zygote has 46 chromosomes and is genetically distinct |
| Cleavage | 30 hours to third day | Mitosis increases cell number |
| Morula | Third to fourth day | Solid ball of cells |
| Blastocyst | Fifth day through second week | Hollow ball consisting of the trophoblast (outside), which implants and helps form the placenta, and inner cell mass, which flattens to form the embryonic disc |
| Gastrula | End of second week | Primary germ layers form |

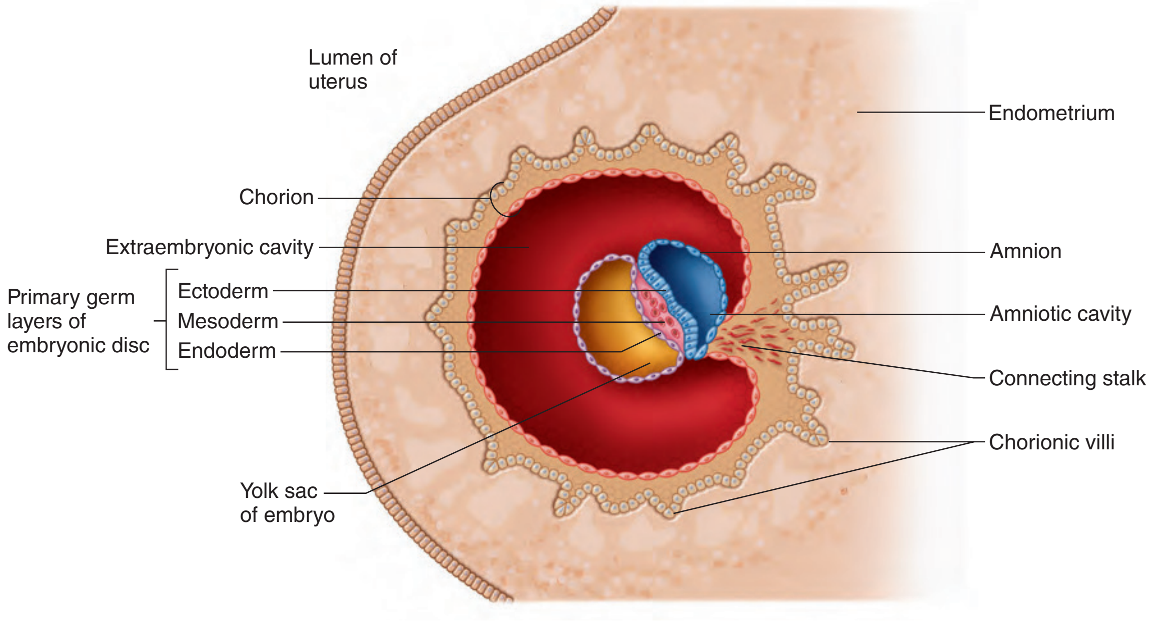

Lumen of uterus
Endometrium
Chorion
Extraembryonic cavity
Amnion
Primary germ layers of embryonic disc
Ectoderm
Mesoderm
Endoderm
Amniotic cavity
Connecting stalk
Chorionic villi
Yolk sac of embryo

**FIGURE 20.7** Early in the embryonic stage of development, the three primary germ layers form. The ectoderm and the endoderm form first, and then the mesoderm forms between them.

week as a tube extending from the early yolk sac into the connecting stalk of the embryo. It, too, forms blood cells and gives rise to the umbilical arteries and vein.

During the fourth week of development, the flat embryonic disc becomes cylindrical to form the neural tube, which will become the central nervous system. By the end of week four, the head and jaws appear, the heart beats and forces blood through the blood vessels, and tiny buds form, which will give rise to the upper and lower limbs (fig. 20.8).

As the embryo becomes more cylindrical, the margins of the amnion fold, enclosing the embryo in the amnion and amniotic fluid. The amnion envelops the tissues on the underside of the embryo, by which the embryo is attached to the chorion and the developing placenta. In this manner, the **umbilical cord** (um-bil′ĭ-kal kord) forms.

The umbilical cord originates at the umbilicus of the embryo and inserts into the center of the placenta (fig. 20.8). It suspends the embryo in the *amniotic cavity*. The umbilical cord contains three blood vessels—two

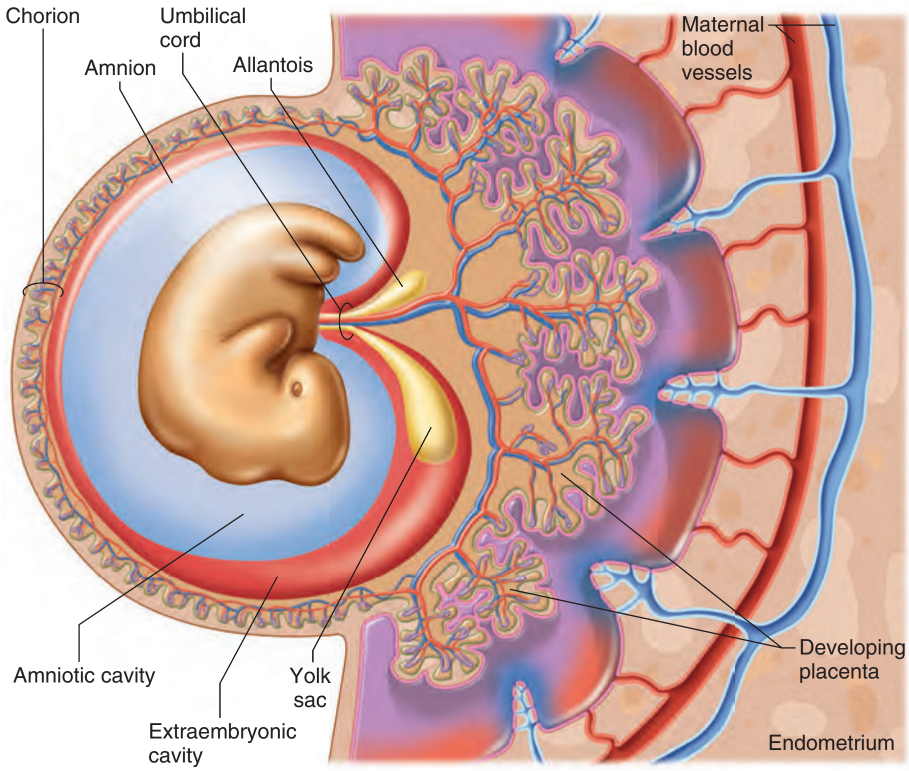

Chorion
Umbilical cord
Amnion
Allantois
Maternal blood vessels
Amniotic cavity
Yolk sac
Extraembryonic cavity
Developing placenta
Endometrium

**FIGURE 20.8** The area where the chorion contacts the uterine wall develops into the placenta.

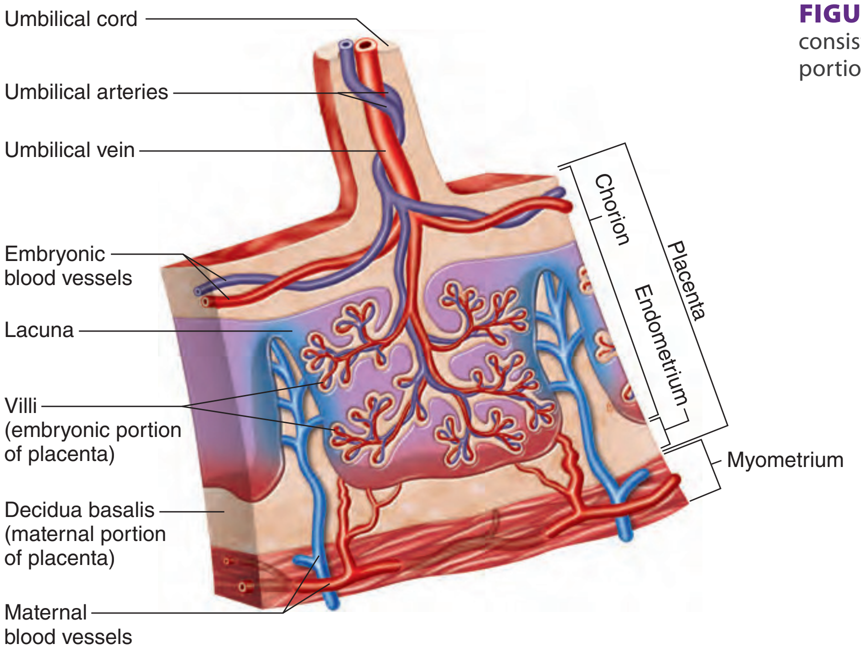

Umbilical cord
Umbilical arteries
Umbilical vein
Embryonic blood vessels
Lacuna
Villi (embryonic portion of placenta)
Decidua basalis (maternal portion of placenta)
Maternal blood vessels
Chorion
Endometrium
Placenta
Myometrium

**FIGURE 20.9** The placenta consists of an embryonic portion and a maternal portion.

*umbilical arteries* and one *umbilical vein*—that transport blood between the embryo and the placenta (fig. 20.9).

The embryonic portion of the placenta is the chorion and its villi; the maternal portion is the area of the uterine wall (decidua basalis) where the villi attach (fig. 20.9). The fully formed placenta is a reddish-brown disc about 20 centimeters long and 2.5 centimeters thick, and weighs about 0.5 kilogram.

A thin **placental membrane** separates embryonic blood in the capillary of a chorionic villus from maternal blood in a lacuna. This membrane is composed of the epithelium of the chorionic villus and the endothelium of the capillary inside the villus. Through this membrane, substances are exchanged between the maternal blood and the embryo's blood (fig. 20.10). Oxygen and nutrients diffuse from the maternal blood into the embryo's blood, and carbon dioxide and other wastes diffuse from the embryo's blood into the maternal blood. Various substances also cross the placental membrane by active transport and pinocytosis.

During the fifth through seventh weeks, as figure 20.11 shows, the head grows rapidly and becomes rounded and erect. The face develops eyes, nose, and mouth. The upper and lower limbs elongate, and fingers and toes form. By the end of the seventh week, all the main internal organs are established. As these structures enlarge, the body takes on a humanlike appearance (fig. 20.12). By the beginning of the eighth week, the embryo is about 30 millimeters long and weighs less than 5 grams.

Until about the end of the eighth week, the chorionic villi cover the entire surface of the former trophoblast. However, as the embryo and the surrounding chorion enlarge, only villi that contact the endometrium endure. The others degenerate, and the areas of the chorion where they were attached become smooth. The region of the chorion still in contact with the uterine wall is restricted to the placenta.

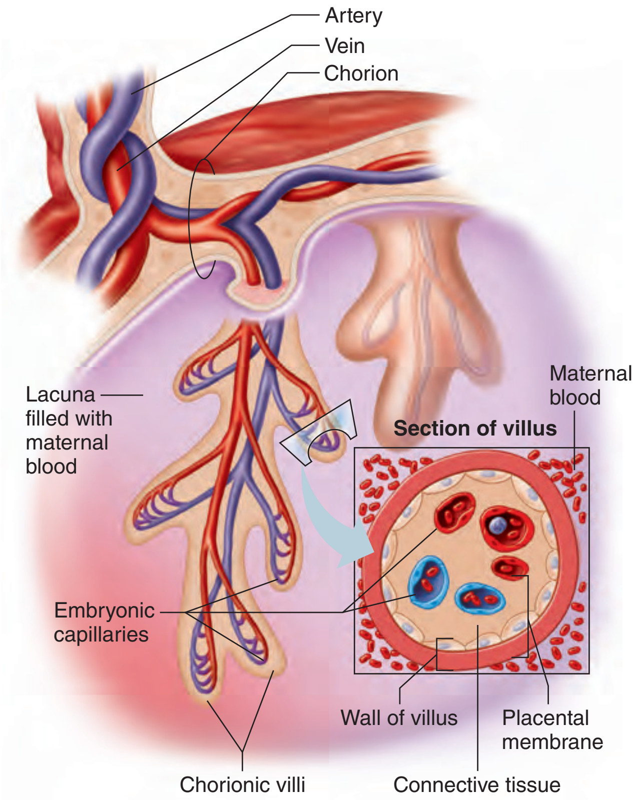

Artery
Vein
Chorion
Lacuna filled with maternal blood
Maternal blood
Section of villus
Embryonic capillaries
Wall of villus
Placental membrane
Chorionic villi
Connective tissue

**FIGURE 20.10** The placental membrane consists of the endothelium of an embryonic capillary and the epithelial wall of a chorionic villus, as illustrated in the section of the villus (lower part of the figure).

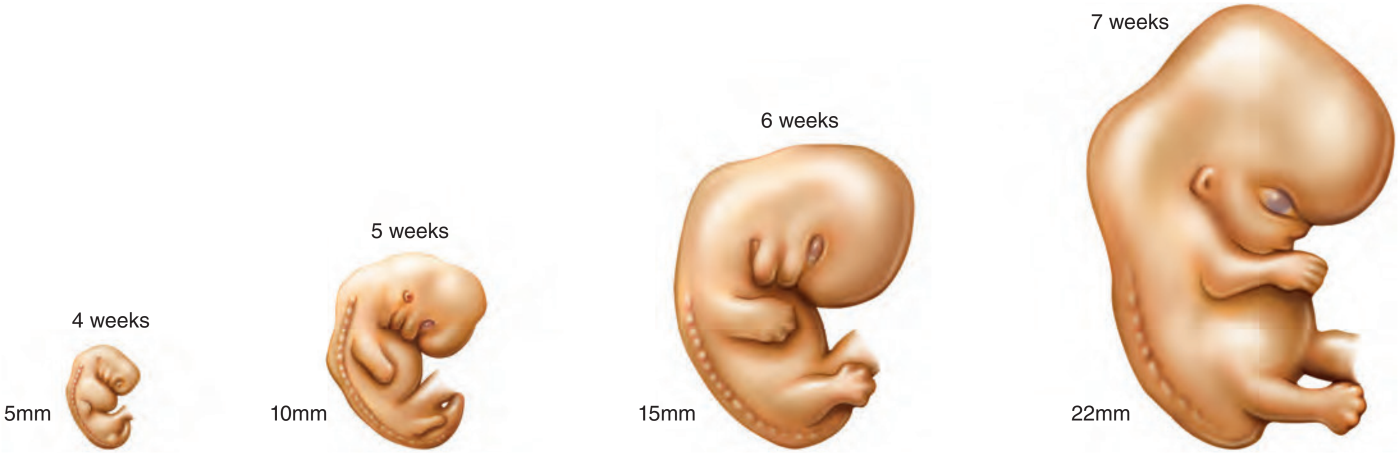


**FIGURE 20.11** In the fifth through the seventh weeks of development, the embryonic body and face develop a humanlike appearance. Actual size indicated in millimeters (mm).

If a pregnant woman repeatedly ingests an addictive substance that crosses the placenta, her newborn may suffer from withdrawal symptoms when amounts of the chemical the fetus was accustomed to receiving suddenly plummet after birth. Newborn addiction occurs with certain drugs of abuse, such as heroin, and with certain prescription drugs used to treat anxiety.

The embryonic stage concludes at the end of the eighth week. It is the most critical period of development when all the essential external and internal body parts form. Factors that cause congenital malformations by affecting an embryo are called **teratogens.** Such agents include drugs, viruses, radiation, and even large amounts of otherwise healthful substances, such as fat-soluble vitamins.

The specific nature of a birth defect reflects the structures developing when the damage occurs. The time during prenatal development when a genetic mutation or exposure to a teratogen can alter a specific structure is called its *critical period.* Clinical Application 20.2 discusses some teratogens.

Some structures, such as fingers and toes, have very short critical periods. In contrast, the brain is sensitive throughout development and even into childhood, so its critical period is very long. This is why many birth defects are associated with the brain, resulting in intellectual impairment.

## PRACTICE

15. What types of cells are derived from the yolk sac?
16. Which blood vessels are in the umbilical cord?
17. What is the function of the placental membrane?
18. What is a teratogen?

## Fetal Stage

The **fetal stage** begins at the end of the eighth week of development and lasts until birth. During this period, growth is rapid and body proportions change considerably. At the beginning of the fetal stage, the head is disproportionately large and the lower limbs are short. Gradually proportions come to more closely resemble those of a child.

During the third month, body lengthening accelerates but head growth slows. The upper limbs achieve the relative length they will maintain throughout development, and ossification centers appear in most bones. By the twelfth week the external reproductive organs are distinguishable as male or female.

In the fourth month the body grows rapidly and reaches a length of up to 20 centimeters. The lower limbs lengthen considerably, and the skeleton continues to ossify. A four-month-old fetus will startle and turn

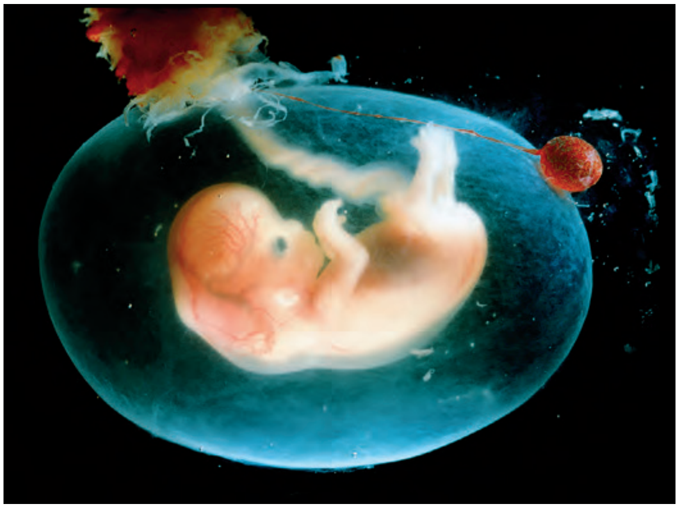


**FIGURE 20.12** By the beginning of the eighth week of development, the embryonic body is recognizable as human.

away from a bright light flashed on a pregnant woman's belly, and may also react to sudden loud noises.

In the fifth month, growth slows. The lower limbs achieve their final relative proportions. Skeletal muscles contract, and the pregnant woman may feel fetal movements. Hair begins to grow on the head. Fine, downy hair and a cheesy mixture of dead epidermal cells and sebum from the sebaceous glands coat the skin.

During the sixth month, the fetus gains substantial weight. Eyebrows and eyelashes grow. The skin is wrinkled and translucent. Blood vessels in the skin cause a reddish appearance.

In the seventh month, the skin becomes smoother as fat is deposited in subcutaneous tissues. The eyelids, which fused during the third month, reopen. At the end of this month the fetus is about 40 centimeters long.

In the final trimester, fetal brain cells rapidly form networks, as organs specialize and grow. A layer of fat is laid down beneath the skin. In the male, the testes descend from regions near the developing kidneys, through the inguinal canal, and into the scrotum. The digestive and respiratory systems mature last, which is why premature infants may have difficulty digesting milk and breathing. Approximately 266 days after a single sperm fertilized a secondary oocyte, a baby is ready to be born. It is *full-term*. It is about 50 centimeters long and weighs 2.7–3.6 kilograms. The skin has lost its downy hair, but sebum and dead epidermal cells still coat it. Hair usually covers the scalp. The fingers and toes have well-developed nails. The skull bones are largely ossified. As figure 20.13 shows, the fetus is usually positioned upside down, with its head toward the cervix.

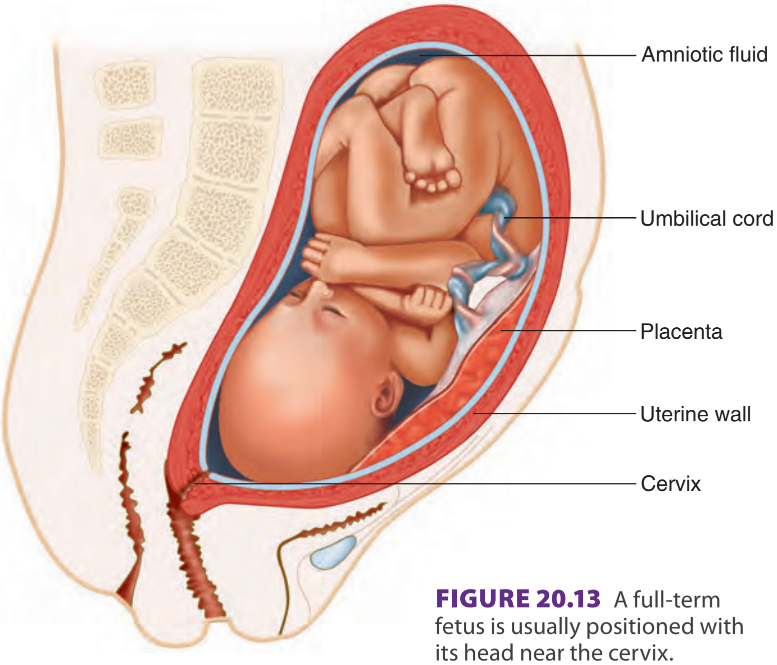


**FIGURE 20.13** A full-term fetus is usually positioned with its head near the cervix.

**PRACTICE**

19. What major changes occur during the fetal stage of development?
20. How is a fetus usually positioned in the uterus as birth nears?

## Fetal Blood and Circulation

Throughout fetal development, the maternal blood supplies oxygen and nutrients and carries away wastes. These substances diffuse between maternal and fetal blood through the placental membrane, and the umbilical blood vessels carry them to and from the fetus.

The fetal blood and cardiovascular system are adapted to the intrauterine environment. The concentration of oxygen-carrying hemoglobin in fetal blood is about 50% greater than in maternal blood, and fetal hemoglobin has a greater attraction for oxygen than does adult hemoglobin. At a particular oxygen partial pressure, fetal hemoglobin can carry 20–30% more oxygen than adult hemoglobin. Different genes encode the protein subunits of hemoglobin in embryos, fetuses, and individuals after birth. The different subunits have different affinities for oxygen.

A treatment for severe sickle cell disease is a drug that reactivates silenced fetal hemoglobin genes. In the disease, adult hemoglobin changes shape under low oxygen conditions, causing red blood cells to distort into a sickle-like shape. The abnormal cells block circulation, causing very painful "crises." Hydroxyurea induces production of the normal fetal hemoglobin subunits, which bind some of the adult hemoglobin subunits, preventing sickling and enabling the red blood cells to circulate to reach the lungs and pick up oxygen. Hydroxyurea decreases the frequency of crises and hospitalizations.

Figure 20.14 shows the path of blood in the fetal cardiovascular system. The umbilical vein transports blood rich in oxygen and nutrients from the placenta to the fetal body. This vein enters the body and travels along the anterior abdominal wall to the liver. About half the blood it carries passes into the liver, and the rest enters a vessel called the **ductus venosus** (duk′tus ve′no-sus), which bypasses the liver.

The ductus venosus extends a short distance and joins the inferior vena cava. There, oxygen-rich blood from the placenta mixes with oxygen-poor blood from the lower parts of the fetal body. This mixture continues through the inferior vena cava to the right atrium.

Postnatally, blood from the right atrium enters the right ventricle and is pumped through the pulmonary

## CLINICAL APPLICATION 20.2

## Some Causes of Birth Defects

### Thalidomide

The idea that the placenta protects the embryo and fetus from harmful substances was tragically disproven between 1957 and 1961, when 10,000 children in Europe were born with malformed, stunted limbs due to exposure to a mild tranquilizer drug, *thalidomide,* during the time of limb formation. Although some women in the United States did use thalidomide and had affected children, the country was spared a larger disaster because an astute government physician noted adverse effects of the drug on monkeys in experiments and halted use of the drug. However, thalidomide is used today to treat leprosy, certain blood disorders, and a type of severe nosebleed.

### Rubella

The virus that causes rubella (German measles) is a powerful teratogen. Exposure in the first trimester leads to cataracts, deafness, and heart defects, and later exposure causes learning disabilities, speech and hearing problems, and type 1 diabetes mellitus. Successful vaccination programs provide for maternal immunity to the virus, and have since greatly lowered the incidence of "congenital rubella syndrome" in many countries.

### Alcohol

A pregnant woman who has just one or two alcoholic drinks a day, or perhaps many drinks at a crucial time in prenatal development, risks *fetal alcohol syndrome (FAS)* in her unborn child. The effects of small amounts of alcohol at different stages of pregnancy are not yet well understood, and because each woman metabolizes alcohol slightly differently, women are advised to avoid drinking alcohol entirely when pregnant or when trying to become pregnant.

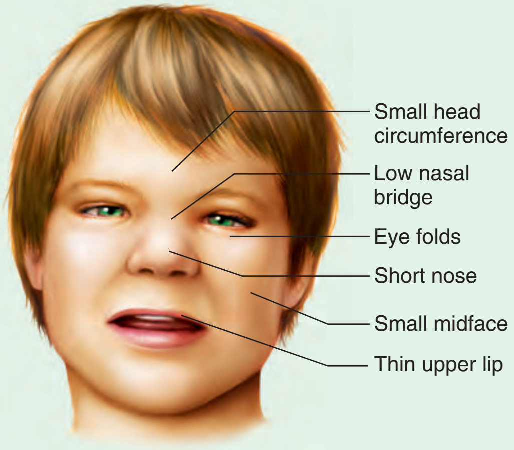


**FIGURE 20A** Fetal alcohol syndrome. Some children whose mothers drank alcohol during pregnancy have characteristic flat faces. Women who drink excessively while pregnant have a 30% to 45% chance of having a child affected to some degree by prenatal exposure to alcohol.

trunk and pulmonary arteries to the lungs (see chapter 13, p. 354 and 356). The fetal lungs, however, are nonfunctional, and blood largely bypasses them. Much of the blood from the inferior vena cava that enters the fetal right atrium is shunted directly into the left atrium through an opening in the atrial septum called the **foramen ovale** (fo-ra′man ova′le). Blood passes through the foramen ovale because the blood pressure is somewhat greater in the right atrium than in the left atrium. Furthermore, flaps of tissue on the left side of the atrial septum overlap the foramen ovale and help prevent blood from moving in the reverse direction.

The rest of the fetal blood entering the right atrium, including a large proportion of the oxygen-poor blood entering from the superior vena cava, passes into the right ventricle and out through the pulmonary trunk. Only a small volume of blood enters the pulmonary circuit because the lungs are collapsed and their blood vessels have a high resistance to blood flow. However, enough blood does reach lung tissues to sustain them.

Most of the blood in the pulmonary trunk bypasses the lungs by entering a fetal vessel called the **ductus arteriosus** (duk′tus ar-te″re-o′sus), which connects the pulmonary trunk to the descending portion of the aortic arch. As a result of this connection, blood with a relatively low oxygen concentration, returning to the heart through the superior vena cava, bypasses the lungs. (This might seem odd, but remember that fetal blood becomes oxygenated in the placenta, not in the fetal lungs.) At the same time, the low-oxygen blood is prevented from entering the portion of the aorta that branches to the heart and brain.

The more highly oxygenated blood that enters the left atrium through the foramen ovale mixes with a small amount of oxygen-poor blood returning from the pulmonary veins. This mixture moves into the left ventricle and is pumped into the aorta. Some of it reaches the myocardium through the coronary arteries, and some reaches the brain tissues through the carotid arteries.

A child with FAS has a small head, misshapen eyes, and a flat face and nose (fig. 20A). Growth is slow before and after birth. Intellect is impaired, ranging from minor learning disabilities to intellectual disability. Many individuals remain at an early grade-school level of intellectual development, and they often lack social and communication skills. People with FAS are also more likely to have seizures.

In the United States today, FAS is the third most common cause of intellectual disability in newborns. Each year in the United States, about 5,000 children are born with FAS, and many more are born with milder "alcohol-related effects."

### Cigarettes

Chemicals in cigarette smoke stress a fetus. Carbon monoxide crosses the placenta and binds to fetal hemoglobin in a way that prevents the hemoglobin from delivering oxygen to the fetal tissues. Other chemicals in smoke prevent nutrients from reaching the fetus. Smoke-exposed placentas lack important growth factors. The result of these assaults is poor growth before and after birth. Cigarette smoking during pregnancy is linked to spontaneous abortion, stillbirth, prematurity, and low birth weight.

### Nutrients and Malnutrition

Certain nutrients in large amounts, particularly vitamins, act in the body as drugs. The acne medication Accutane (*isotretinoin*) is a derivative of vitamin A that causes spontaneous abortions and defects of the fetal heart, nervous system, and face. A vitamin A–based drug used to treat psoriasis, as well as excesses of vitamin A itself, also cause birth defects because some forms of the vitamin are stored in body fat for up to three years after ingestion.

Malnutrition during pregnancy causes intrauterine growth retardation (IUGR). Malnutrition before birth also causes shifts in metabolism to make the most of calories from food. This protective action, however, sets the stage for developing obesity and associated disorders, such as type 2 diabetes and cardiovascular disease, in adulthood.

### Occupational Hazards

The workplace can be a source of teratogens. Women who work with textile dyes, lead, certain photographic chemicals, semiconductor materials, mercury, and cadmium have increased rates of spontaneous abortion and delivering children with birth defects. Men whose jobs expose them to sustained heat, such as smelter workers, glass manufacturers, and bakers, may produce sperm that can fertilize a secondary oocyte, but possibly lead to spontaneous abortion or a birth defect. A virus or a toxic chemical carried in semen may also cause a birth defect.

Blood carried by the descending aorta includes the less oxygenated blood from the ductus arteriosus. Some of the blood is carried into the branches of the aorta that lead to the lower regions of the body. The rest passes into the umbilical arteries, which branch from the internal iliac arteries and lead to the placenta. There the blood is reoxygenated (fig. 20.14).

Table 20.4 summarizes the major features of fetal circulation. At the time of birth, important adjustments must occur in the fetal cardiovascular system when the placenta ceases to function and the newborn begins to breathe.

The umbilical cord usually contains two arteries and one vein. On rare occasion a newborn will have only one umbilical artery. Because this condition is often associated with other cardiovascular disorders, the vessels in the severed cord are routinely counted following birth.

**TABLE 20.4** Fetal Cardiovascular Adaptations

| Adaptation | Function |
|---|---|
| Fetal blood | Hemoglobin has greater oxygen-carrying capacity than adult hemoglobin |
| Umbilical vein | Carries nutrient-rich, oxygen-rich blood from placenta to fetus |
| Ductus venosus | Conducts about half the blood from the umbilical vein directly to the inferior vena cava, bypassing the liver |
| Foramen ovale | Conveys a large portion of the blood entering the right atrium from the inferior vena cava, through the atrial septum, and into the left atrium, bypassing the lungs |
| Ductus arteriosus | Conducts some blood from the pulmonary trunk to the aorta, bypassing the lungs |
| Umbilical arteries | Carry blood containing carbon dioxide and wastes from the internal iliac arteries to the placenta |

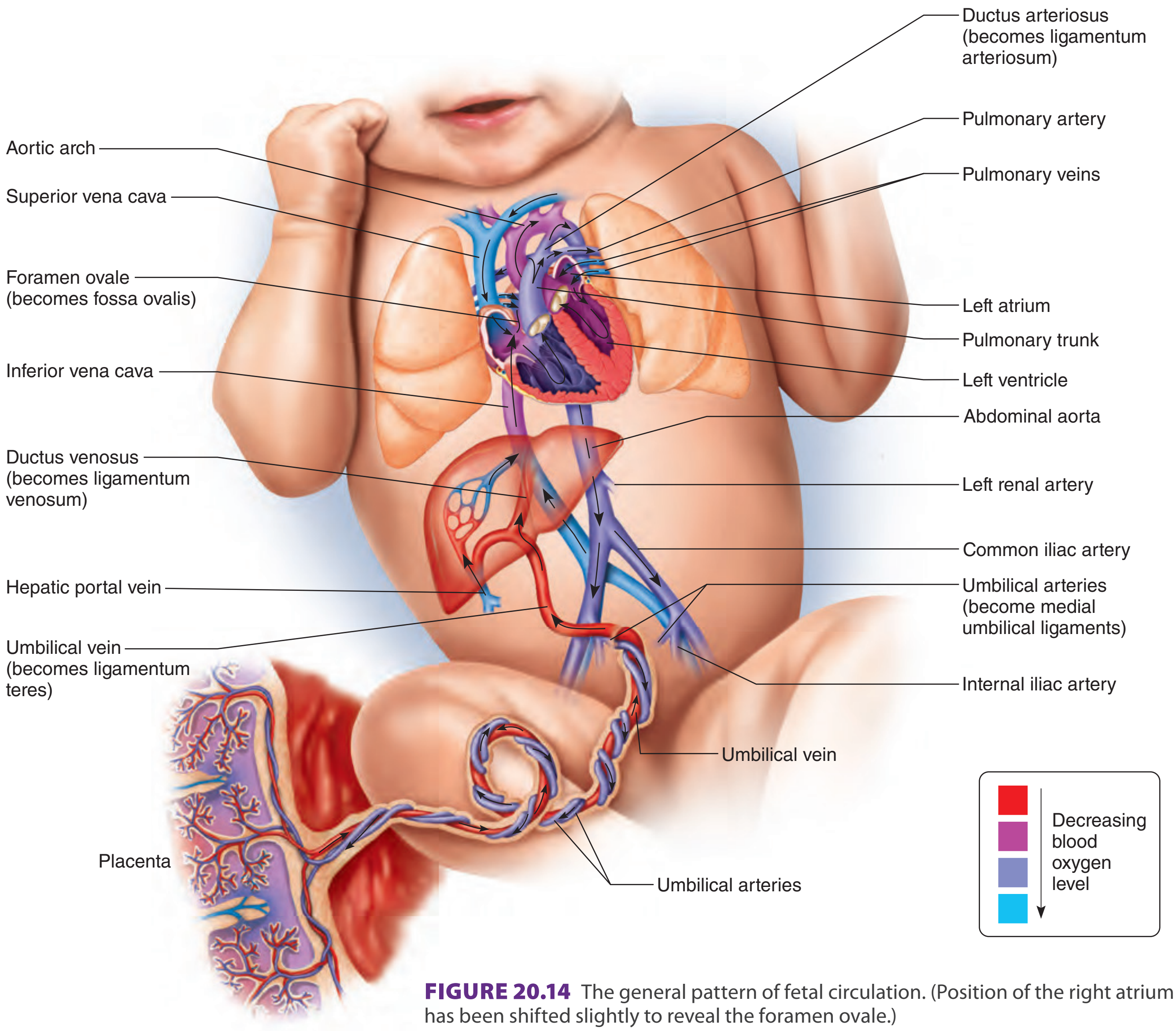

Ductus arteriosus (becomes ligamentum arteriosum)
Pulmonary artery
Pulmonary veins
Aortic arch
Superior vena cava
Foramen ovale (becomes fossa ovalis)
Left atrium
Pulmonary trunk
Inferior vena cava
Left ventricle
Abdominal aorta
Ductus venosus (becomes ligamentum venosum)
Left renal artery
Common iliac artery
Hepatic portal vein
Umbilical arteries (become medial umbilical ligaments)
Umbilical vein (becomes ligamentum teres)
Internal iliac artery
Umbilical vein
Decreasing blood oxygen level
Placenta
Umbilical arteries

**FIGURE 20.14** The general pattern of fetal circulation. (Position of the right atrium has been shifted slightly to reveal the foramen ovale.)

Q *Which structures are unique to the fetal circulation?*
**Answer can be found in Appendix F on page 582.**

**PRACTICE**

21. Which umbilical vessel carries oxygen-rich blood to the fetus?
22. What is the function of the ductus venosus?
23. How does fetal circulation allow blood to bypass the lungs?

## Birth Process

Pregnancy usually continues for thirty-eight weeks from conception and ends with the *birth process.* During pregnancy, progesterone suppresses uterine contractions. As the placenta ages, the progesterone concentration in the uterus declines, which stimulates synthesis of a prostaglandin that promotes uterine contractions. At the same time, the cervix thins and then opens. Changes in the cervix may begin a week or two before other signs of labor appear.

Stretching of the uterine and vaginal tissues late in pregnancy also stimulates the birth process. This action initiates impulses to the hypothalamus, which in turn signals the posterior pituitary gland to release the hormone **oxytocin** (see chapter 11, pp. 309–310). Oxytocin stimulates powerful uterine contractions. Combined with the greater excitability of the myometrium due to the decline in progesterone secretion, stimulation by oxytocin aids *labor* in its later stages.

During labor, rhythmic muscular contractions begin at the top of the uterus and travel down its length. Because the fetus is usually positioned head downward, labor contractions force the head against the cervix (fig. 20.15). This action stretches the cervix, which elicits a reflex that stimulates stronger labor contractions. Thus a *positive feedback system* operates in which uterine contractions produce more intense uterine contractions

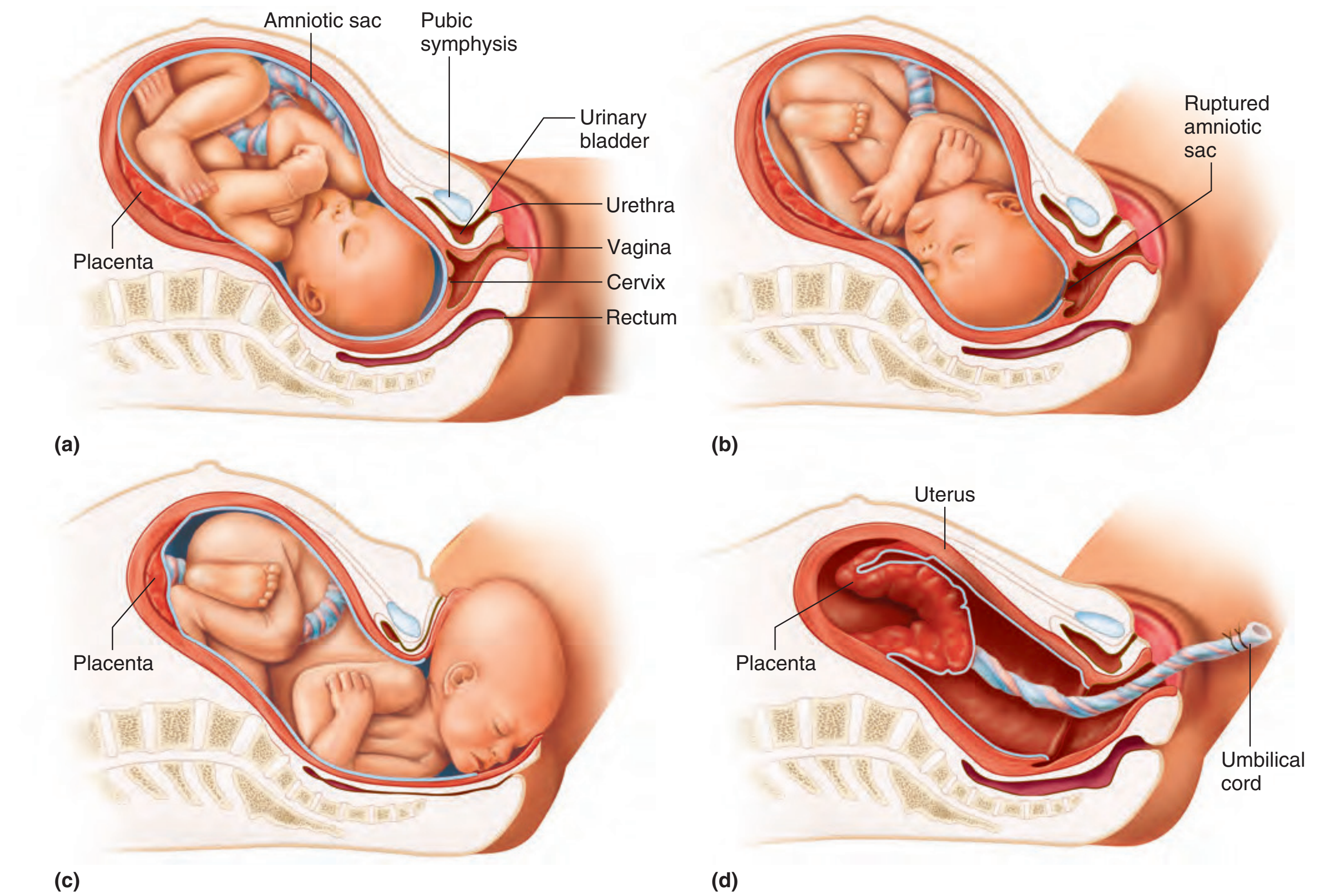


**FIGURE 20.15** Stages in birth. (**a**) Fetal position before labor, (**b**) dilation of the cervix, (**c**) expulsion of the fetus, (**d**) expulsion of the placenta.

until contractions are maximal. At the same time, dilation of the cervix reflexly stimulates the posterior pituitary to increase oxytocin release. As labor continues, positive feedback stimulates abdominal wall muscles to contract, helping to propel the fetus through the cervix and vagina to the outside.

An infant passing through the birth canal can stretch and tear the delicate tissues between the vulva and anus (perineum). To avoid a ragged tear, a physician may make an *episiotomy,* which is a clean cut in the perineal tissues.

Following birth of the fetus, the placenta separates from the uterine wall and is pushed by uterine contractions through the birth canal. This expelled placenta, called the *afterbirth,* is accompanied by bleeding, because vascular tissues are damaged in the process. However, oxytocin stimulates continued uterine contraction, which compresses the bleeding vessels and minimizes blood loss. Breastfeeding also contributes to returning the uterus to its original, prepregnancy size, because suckling by the newborn stimulates the mother's posterior pituitary gland to release oxytocin.

**PRACTICE**

24. Describe the role of progesterone in initiating labor.
25. Explain how dilation of the cervix affects labor.

## Milk Production and Secretion

During pregnancy, placental estrogens and progesterone stimulate further development of the mammary glands. Estrogens cause the ductile systems to grow and branch and deposit abundant fat around them. Progesterone stimulates the development of the alveolar glands at the ends of the ducts. Placental lactogen also promotes these changes.

The breasts may double in size during pregnancy because of hormonal action. Mammary glands become capable of secreting milk. However, milk secretion does not begin until after birth, because placental progesterone inhibits milk production and placental lactogen blocks the action of *prolactin* (see chapter 11, pp. 308–309). Prolactin is synthesized from early pregnancy throughout gestation, peaking at birth.

Following childbirth and the expulsion of the placenta, maternal blood concentrations of placental hormones decline rapidly. The action of prolactin is no longer inhibited. Prolactin stimulates the mammary glands to secrete milk. This hormonal effect does not occur until two or three days following birth. In the meantime, the glands secrete a thin, watery fluid called *colostrum* that has more protein, but less carbohydrate and fat, than milk. Colostrum contains antibodies from the mother's immune system that protect the newborn from certain infections.

Milk ejection requires contraction of specialized *myoepithelial cells* surrounding the alveolar glands (fig. 20.16). Suckling or mechanical stimulation of sensory receptors in the nipple or areola elicits the reflex action that controls this process. Impulses from these receptors go to the hypothalamus, which signals the posterior pituitary gland to release oxytocin. Oxytocin travels in the bloodstream to the breasts and stimulates the myoepithelial cells to contract. Within about thirty seconds, milk squirts into a suckling infant's mouth.

As long as milk is removed from the breasts, release of prolactin and oxytocin continues, and the mammary glands produce milk. If milk is not removed regularly, the hypothalamus inhibits prolactin secretion, and within about one week the mammary glands stop producing milk.

Human milk is the best possible food for human babies. The milk of other mammals contains different proportions of nutrients.

Human milk is 4.5% fat and 1.1% protein, which is suitable for supporting synthesis of myelin, the fatty electrical insulation that enables neurons in the developing brain to communicate effectively. In contrast, cow's milk has 3.5% fat and 3.1% protein, because it is more important for survival for the calf to bulk up its muscles than to develop its brain.

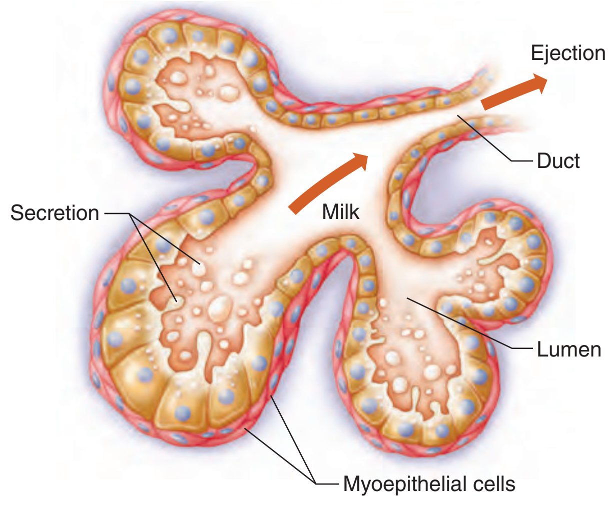


**FIGURE 20.16** Myoepthelial cells contract, releasing milk from an alveolar gland.

**PRACTICE**

26. How does pregnancy affect the mammary glands?
27. What stimulates the mammary glands to produce milk?
28. What causes milk ejection?

## 20.4 | Postnatal Period

Following birth, the newborn experiences physiological and structural changes. The postnatal period of development lasts from birth to death.

### Neonatal Period

The **neonatal** (ne″o-na′tal) **period** begins abruptly at birth and extends to the end of the first four weeks. At birth, the newborn must make quick physiological adjustments to become self-reliant. It must respire, obtain and digest nutrients, excrete wastes, and regulate body temperature.

A newborn's most immediate need is to obtain oxygen and excrete carbon dioxide. The first breath must be particularly forceful, because the newborn's lungs are collapsed and the airways are small, offering considerable resistance to air movement. Also, surface tension holds the moist membranes of the lungs together. However, the lungs of a full-term fetus continuously secrete *surfactant* (see chapter 16, p. 463), which reduces surface tension. After the first powerful inhalation inflates the lungs, breathing eases.

Premature infants' survival chances increase directly with age and weight, and parallel the increasing maturity of the lungs. The ability of the alveoli to exchange gases and the presence of surfactant to reduce alveolar surface tension are important. A baby born at twenty-five weeks has a 50% chance of survival; at twenty-four weeks, a 39% chance; and at twenty-three weeks, a 17% chance.

The newborn has a high metabolic rate. To supplement the liver's supply of glucose to support metabolism, the newborn typically utilizes stored fat for energy.

A newborn's kidneys are usually unable to concentrate urine, so the baby excretes dilute urine. This may cause dehydration and a water and electrolyte imbalance. Also, certain homeostatic control mechanisms may not function adequately. For example, during the first few days of life, body temperature may respond to slight stimuli by fluctuating above or below normal levels.

When the placenta ceases to function and breathing begins, the newborn's cardiovascular system changes. Following birth, the umbilical vessels constrict. The umbilical arteries close first, and if the umbilical cord is not clamped or severed for a minute or so, blood continues to flow from the placenta to the newborn through the umbilical vein, adding to the newborn's blood volume. Similarly, the ductus venosus constricts shortly after birth and appears in the adult as a fibrous cord (ligamentum venosum) superficially embedded in the wall of the liver.

The foramen ovale closes as a result of blood pressure changes in the right and left atria. As blood ceases to flow from the umbilical vein into the inferior vena cava, the blood pressure in the right atrium falls. Also, as the lungs expand with the first breathing movements, resistance to blood flow through the pulmonary circuit decreases, more blood enters the left atrium through the pulmonary veins, and blood pressure in the left atrium increases.

As the blood pressure in the left atrium rises and that in the right atrium falls, the tissue flaps on the left side of the atrial septum close the foramen ovale. In most individuals the tissue flaps gradually fuse with the tissues along the margin of the foramen. In an adult, a depression called the *fossa ovalis* marks the site of the past opening.

The ductus arteriosus, like the other fetal vessels, constricts after birth. After this, blood can no longer bypass the lungs by moving from the pulmonary trunk directly into the aorta. In an adult, a cord called the *ligamentum arteriosum* represents the ductus arteriosus.

Changes in the newborn's cardiovascular system are gradual. Although constriction of the ductus arteriosus may be functionally complete within fifteen minutes, the permanent closure of the foramen ovale may take up to a year.

In *patent ductus arteriosus (PDA),* the ductus arteriosus fails to close completely. After birth, the metabolic rate and oxygen consumption in neonatal tissues increase. If the ductus arteriosus remains open, bypassing the pulmonary circuit, the neonate's blood oxygen concentration may be too low to adequately supply tissues, including the myocardium. If PDA is not corrected surgically, the heart may fail, even though the myocardium is normal.

Fetal hemoglobin production falls after birth, and by the time an infant is four months old, most of the circulating hemoglobin is the adult type. Figure 20.17 illustrates cardiovascular changes in the newborn. Table 20.5 summarizes the major events during the neonatal period as well as those of the later stages of human development.

## PRACTICE

29. Why must a newborn's first breath be particularly forceful?
30. What does a newborn use for energy during its first few days?
31. How do the kidneys of a newborn differ from those of an adult?
32. What changes occur in the newborn's cardiovascular system?

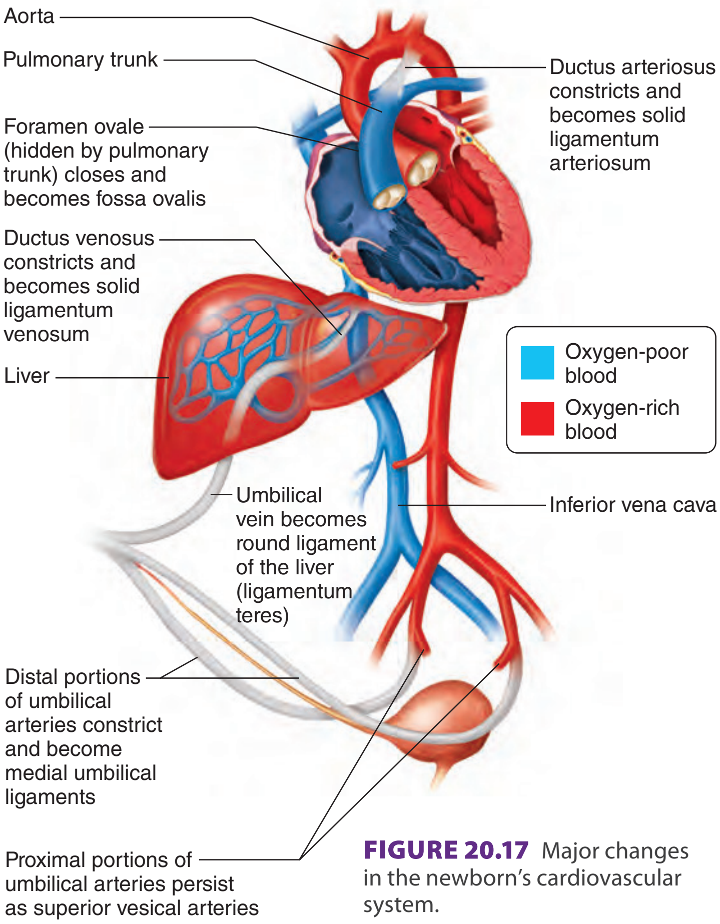

Aorta
Pulmonary trunk
Foramen ovale (hidden by pulmonary trunk) closes and becomes fossa ovalis
Ductus venosus constricts and becomes solid ligamentum venosum
Liver
Umbilical vein becomes round ligament of the liver (ligamentum teres)
Distal portions of umbilical arteries constrict and become medial umbilical ligaments
Proximal portions of umbilical arteries persist as superior vesical arteries
Ductus arteriosus constricts and becomes solid ligamentum arteriosum
🟦 Oxygen-poor blood
🟥 Oxygen-rich blood
Inferior vena cava

**FIGURE 20.17** Major changes in the newborn's cardiovascular system.

## 20.5 | Aging

The aging process is difficult to analyze because of the intricate interactions of the body's organ systems. Breakdown of one structure ultimately affects the functioning of others. Table 20.6 outlines aging-related changes.

### Passive Aging

Aging as a passive process is the breakdown of structures and slowing of function. At the molecular level, passive aging is seen in the degeneration of the elastin and collagen proteins of connective tissues, causing skin to sag and muscle to lose its firmness.

During a long lifetime, biochemical abnormalities accumulate. Mistakes occur throughout life when DNA replicates in dividing cells. Usually repair enzymes correct this damage immediately. But over many years, exposure to chemicals, viruses, and radiation disrupts DNA repair mechanisms so that the error burden becomes too great to be fixed. The cells may die as a result of faulty genetic instructions.

Another sign of passive aging at the biochemical level is the breakdown of lipids. As aging membranes leak during lipid degeneration, a fatty, brown pigment called lipofuscin accumulates. Mitochondria also begin to break down in older cells, decreasing the supply of chemical energy to power the cell's functions.

### TABLE 20.5 Stages in Postnatal Development

| Stage | Time Period | Major Events |
|---|---|---|
| Neonatal period | Birth to end of fourth week | Newborn begins to respire, eat, digest nutrients, excrete wastes, regulate body temperature, and make cardiovascular adjustments |
| Infancy | End of fourth week to one year | Growth rate is high; teeth begin to erupt; muscular and nervous systems mature so that coordinated activities are possible; communication begins |
| Childhood | One year to puberty | Growth rate is high; primary teeth erupt and are then replaced by secondary teeth; high degree of muscular control is achieved; bladder and bowel controls are established; intellectual abilities mature |
| Adolescence | Puberty to adulthood | Person becomes reproductively functional and emotionally more mature; growth spurts occur in skeletal and muscular systems; high levels of motor skills are developed; intellectual abilities increase |
| Adulthood | Adolescence to old age | Person remains relatively unchanged anatomically and physiologically; degenerative changes begin to occur |
| Senescence | Old age to death | Degenerative changes continue; body becomes less able to cope with demands; death usually results from mechanical disturbances in the cardiovascular system or from diseases that affect vital organs |

### TABLE 20.6 Aging-Related Changes

| Organ System | Aging-Related Changes |
|---|---|
| Integumentary system | Degenerative loss of collagen and elastic fibers in dermis; decreased production of pigment in hair follicles, hair eventually turns white; reduced activity of sweat and sebaceous glands; skin thins, wrinkles, and becomes drier |
| Skeletal system | Degenerative loss of bone matrix; bones become thinner, less dense, and more likely to fracture; stature may shorten due to compression of intervertebral discs and vertebrae |
| Muscular system | Loss of skeletal muscle fibers; degenerative changes in neuromuscular junctions; loss of muscular strength |
| Nervous system | Degenerative changes in neurons; loss of dendrites and synaptic connections; accumulation of lipofuscin in neurons; decreases in sensation; decreasing efficiency in processing and recalling information; decreasing ability to communicate; diminished sense of smell and taste; loss of elasticity of lenses and consequent loss of ability to accommodate for close vision |
| Endocrine system | Reduced hormonal secretions; decreased metabolic rate; reduced ability to cope with stress; reduced ability to maintain homeostasis |
| Cardiovascular system | Degenerative changes in cardiac muscle; decrease in lumen diameters of arteries and arterioles; decreased cardiac output; increased resistance to blood flow; increased blood pressure |
| Lymphatic system | Decrease in efficiency of immune system; increased incidence of infections and neoplastic diseases; increased incidence of autoimmune diseases |
| Digestive system | Decreased motility in gastrointestinal tract; reduced secretion of digestive juices; reduced efficiency of digestion |
| Respiratory system | Degenerative loss of elastic tissue in lungs; fewer alveoli; reduced vital capacity; increase in dead air space; reduced ability to clear airways by coughing |
| Urinary system | Degenerative changes in kidneys; fewer functional nephrons; reductions in filtration rate, tubular secretion, and tubular reabsorption |
| Reproductive systems | |
| Male | Reduced secretion of sex hormones; enlargement of prostate gland; decrease in sexual energy |
| Female | Degenerative changes in ovaries; decrease in secretion of sex hormones; menopause; regression of secondary sex characteristics |

The cellular degradation associated with aging may be set into action by highly reactive chemicals called **free radicals.** A molecule that is a free radical has an unpaired electron in its outermost valence shell. This causes the molecule to grab electrons from other molecules, destabilizing them, and a chain reaction of chemical instability begins that could kill the cell. Free radicals are a by-product of normal metabolism and also form by exposure to radiation or toxic chemicals.

## Active Aging

Aging also entails new activities or the appearance of new substances. Lipofuscin granules, for example, may be considered an active sign of aging, but they result from the passive breakdown of lipids. Another example of active aging is autoimmunity, in which the immune system turns against the body, attacking its cells as if they were invading organisms.

Active aging begins before birth, as certain cells die as part of the developmental program encoded in the genes. This process of programmed cell death, called **apoptosis** (ayp-o-toe′sis), occurs regularly in the embryo, degrading certain structures to pave the way for new ones. The number of neurons in the fetal brain, for example, is halved as those that make certain synaptic connections are spared from death. Throughout life, apoptosis enables organs to maintain their characteristic shapes.

Mitosis and apoptosis are opposite, but complementary, processes. As organs grow, the number of cells in some regions increases, but in others, the number decreases. Cell death is not a phenomenon only of the aged. It is a normal part of life.

### PRACTICE

33. How is aging a passive process?
34. How is aging an active process?

## 20.6 | Genetics

The newborn enters the world, and the elated parents look for family resemblances. Does she have her father's nose, or her grandmother's curly hair?

As the child grows, a unique mix of traits emerges. Inherited traits are determined by DNA sequences that comprise genes, which instruct cells to synthesize particular proteins, as discussed in chapter 4, section 4.6 (pp. 96–100). When a gene's DNA sequence changes, or *mutates,* illness may result. The Genetics Connection features in chapters 3 (p. 68), 8 (p. 203), and 16 (p. 459) describe illnesses that arise from mutations.

The field of **genetics** (jĕ-net′iks) investigates how genes confer specific characteristics that affect health or contribute to our natural variation, and how genes are passed from generation to generation. As discussed in Genetics Connection 20.1, fetal chromosome checks provide clues to an individual's future health. The environment influences how most genes are expressed. For example, inherited gene variants that confer susceptibility to lung cancer might affect health only if a person smokes or is exposed to air pollution for many years.

### Chromosomes and Genes Are Paired

Chromosome charts called karyotypes display the 23 chromosome pairs of a human somatic cell in size order (fig. 20.18). Pairs 1 through 22 are **autosomes** (aw′to-somz), which do not carry genes that determine sex. The other two chromosomes, the X and the Y, include genes that determine sex and are called **sex chromosomes.** A female has two X chromosomes, and a male has one X and one Y.

Each chromosome except the tiny Y includes hundreds of genes. Somatic cells have two copies of each autosome, and therefore two copies of each gene. Gene copies can be identical or slightly different in DNA sequence. Such variant forms of a gene are called **alleles** (ah-léels). An individual who has two identical alleles of a gene is **homozygous** (ho″mo-zi′gus) for that gene. A person with two different alleles is **heterozygous** (het′er-o-zi′gus) for it.

The combination of alleles, for one gene or many, constitutes a person's **genotype** (jē′no-tīp). The appearance, health condition, or other characteristics

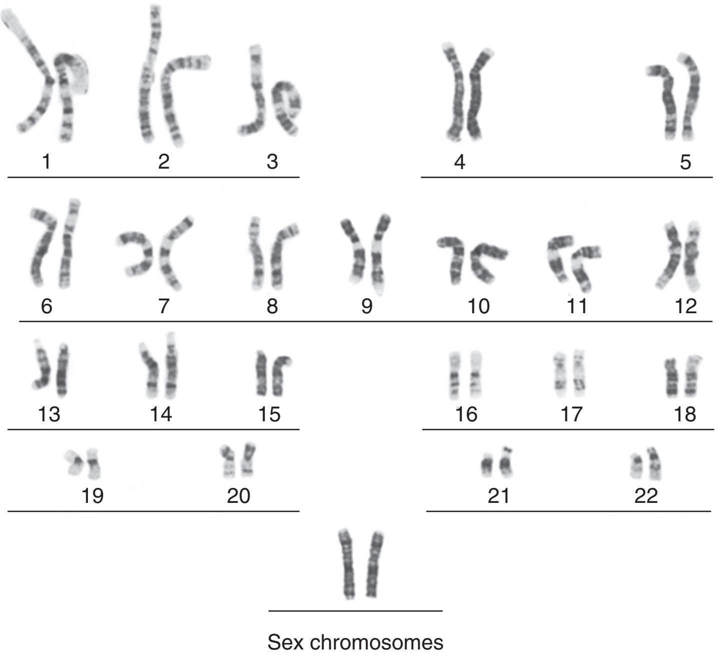


**FIGURE 20.18** A normal human karyotype. Each somatic cell has 22 pairs of autosomes and a pair of sex chromosomes. The two X chromosomes indicate that this size-order chromosome chart (karyotype) is from a female.

## GENETICS CONNECTION 20.1

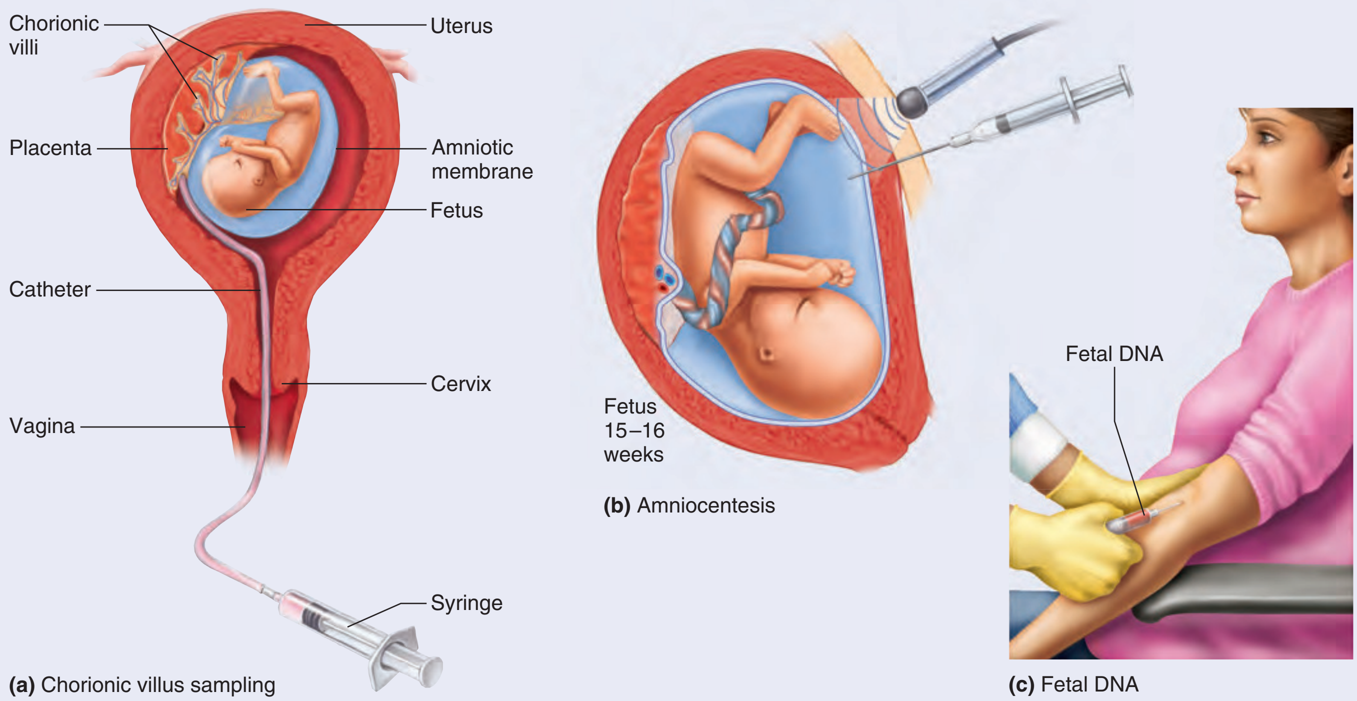
## Fetal Chromosome Checks

Chromosomes provide clues to health. A chromosome number other than 46 usually signals a serious medical condition, as do chromosomes that have missing or extra material. Sampling cells from a fetus and preparing charts of the chromosomes can detect these conditions.

Ultrasound, in which sound waves bounced off a structure are converted into an image, can reveal fusion of the eyes, cleft lip and/or palate, malformed nose, and extra fingers and toes that are part of certain chromosomal syndromes, and many other anomalies. Also, a blood test performed on the woman during the fifteenth week of pregnancy detects levels of certain biomarkers called maternal serum markers (alpha fetoprotein, an estrogen, pregnancy-associated plasma protein A, and human chorionic gonadotropin). (Clinical Application 2.2 on page 57 discusses biomarkers.) Abnormal levels of maternal serum markers may indicate increased risk of an extra chromosome. Doctors follow up questionable ultrasound or blood test results or a family history of abnormal chromosomes with one of the following procedures, which examine fetal chromosomes.

### Chorionic Villus Sampling

*Chorionic villus sampling (CVS)* (fig. 20Ba) examines the chromosomes in chorionic villus cells, which are genetically identical to fetal cells because they are derived from the same fertilized egg. On rare occasion the test causes spontaneous abortion. Due to this risk, women are advised to have the procedure only if they have previously had a child with a detectable chromosome abnormality and therefore have a higher risk of having a detectable problem than the risk of the test itself. CVS is performed at the tenth week of gestation.



**(a)** Chorionic villus sampling

**(b)** Amniocentesis

**(c)** Fetal DNA

**FIGURE 20B** Three ways to check a fetus's chromosomes. (**a**) Chorionic villus sampling (CVS) removes cells of the chorionic villi, whose chromosomes match those of the fetus. (**b**) Amniocentesis withdraws amniotic fluid, which contains fetal cells. (**c**) Some chromosomal conditions can be inferred by analyzing fetal DNA in the maternal circulation. For CVS and amniocentesis, fetal chromosomes are stained and examined. Additional tests are required to detect mutations that cause specific genetic disorders.

associated with a particular genotype is the **phenotype** (fe′no-tīp). An allele is *wild type* (indicated with a plus sign) if its associated phenotype is either normal function or the most common expression in a particular population. An allele that differs from wild type has undergone a mutation, which may lead to a *mutant* (abnormal or unusual) phenotype.

### PRACTICE

35. Distinguish between autosomes and sex chromosomes.
36. How does a homozygote differ from a heterozygote?
37. Distinguish between genotype and phenotype.

### Amniocentesis

*Amniocentesis* is performed after the fourteenth week of gestation. A physician uses ultrasound to guide a needle into the amniotic sac and withdraws about 5 milliliters of fluid (fig. 20B*b*). Fetal fibroblasts in the sample are cultured and their chromosomes are checked. It takes about a week to grow these cells, but a test using fluorescent dyes is used to detect the most common extra-chromosome conditions within 48 hours.

Until recently, amniocentesis carried a risk of about 0.5% of being followed by spontaneous abortion. But the procedure has become much safer. Previously amniocentesis was offered only to women over age thirty-five, when the risk of conceiving a fetus with abnormal chromosomes is about 0.5% (risk increases with age), and women who had already had a child with a detectable chromosomal abnormality. Some medical practices offer the test earlier in pregnancy because of the improvement in safety.

### Fetal DNA in Maternal Circulation

Tests on fetal DNA collected from a pregnant woman's bloodstream are much less invasive, and therefore safer, than sampling cells from the chorionic villi or amniotic fluid. The maternal circulation normally contains pieces of fetal DNA, which can be separated because they are shorter than maternal DNA pieces. The first clinically available prenatal test using fetal DNA is for trisomy 21, the form of Down syndrome caused by an extra chromosome. A karyotype is not constructed, because the test identifies ratios of certain DNA sequences that indicate the extra chromosome.

Entire fetal genomes have been sequenced from DNA pieces in maternal circulation. This technology may become a routine way to detect genetic disease before birth. It is likely that in the coming years, seeking clues to fetal health in the maternal bloodstream may replace the more invasive, older techniques.

### Preimplantation Genetic Diagnosis (PGD)

If a couple has a family history of a chromosomal or single gene condition that could affect their offspring, a procedure called preimplantation genetic diagnosis (PGD) can allow them to select early pre-embryos that have not inherited the condition (fig. 20C). After secondary oocytes are fertilized *in vitro* and allowed to divide to the 8-celled stage, one cell from each of several pre-embryos is removed and tested for the disease-causing mutation or chromosome abnormality. If the genes or chromosomes are unaffected, a tested 7-celled pre-embryo is allowed to continue development *in vitro* before it is introduced into the woman. PGD has enabled thousands of children to be born free of inheriting a disease-causing genotype.

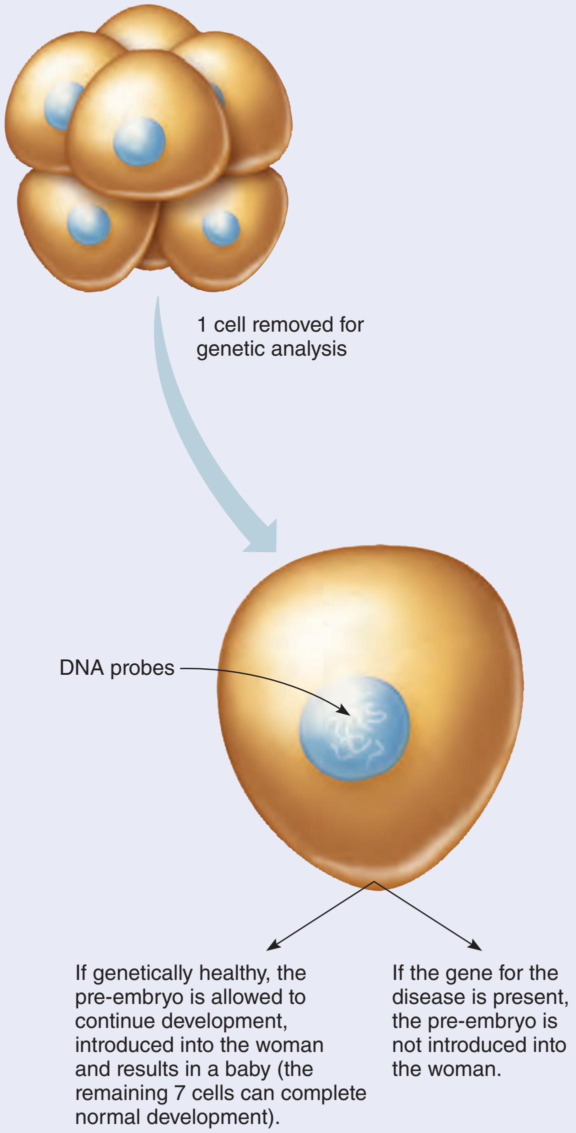

1 cell removed for genetic analysis
DNA probes
If genetically healthy, the pre-embryo is allowed to continue development, introduced into the woman and results in a baby (the remaining 7 cells can complete normal development).
If the gene for the disease is present, the pre-embryo is not introduced into the woman.

**FIGURE 20C** Preimplantation genetic diagnosis detects disease-causing genotypes in an 8-celled pre-embryo.

## Modes of Inheritance

We can predict the probability that a certain inherited trait will occur in the offspring of two individuals by considering how genes and chromosomes are distributed in meiosis, and the combinations in which they can unite at fertilization. Patterns in which genes are transmitted in families are called *modes of inheritance*.

### *Dominant and Recessive Inheritance*

A **dominant** allele masks expression of a **recessive** allele. Dominant alleles are usually indicated with a capital letter. An allele that causes a trait or disease can be recessive or dominant, and inherited in either an autosomal or an X-linked manner. Y-linked conditions are extremely rare because that chromosome has very few genes.

The following generalizations describe modes of inheritance:

1. An autosomal condition affects both sexes. X-linked characteristics affect males much more than females. Y-linked traits are passed only from father to son.
2. A person can inherit an autosomal recessive condition from two healthy heterozygous (carrier) parents. For this reason, recessive conditions can "skip" generations. Or a person can inherit this condition from a homozygous recessive parent and a heterozygous parent. In this case the homozygous recessive parent has the condition.
3. A person who inherits a dominant condition has at least one affected parent. Therefore, generations are not skipped.

Three major modes of inheritance are autosomal recessive, autosomal dominant, and X-linked recessive. Cystic fibrosis illustrates *autosomal recessive* inheritance, in which two recessive alleles, one from each parent, transmit a trait. Receiving two disease-causing alleles impairs chloride channels in cells lining the pancreas, respiratory tract, intestines, and testes (see Genetics Connection 16.1, p. 459). Half of a heterozygous man's sperm have the disease-causing allele, as do half of the woman's secondary oocytes. Because sperm and oocytes combine at random, each offspring has a 25% chance of inheriting two wild type alleles, a 50% chance of inheriting a disease-causing allele from either parent and being a carrier, and a 25% chance of inheriting a disease-causing allele from each parent.

Figure 20.19 illustrates two ways to depict the possible offspring of two carriers of cystic fibrosis. A **Punnett square** symbolizes the logic used to deduce the probabilities of inheriting particular genotypes in offspring. Each box records an allele combination at fertilization. A **pedigree** is a diagram that depicts family members, how they are related, and their genotypes. Males are squares, females are circles, and the symbols for carriers are half filled in while those for affected individuals are entirely filled in. Geneticists use Punnett squares and pedigrees to predict the outcome in all modes of inheritance.

Only one disease-causing allele is necessary to inherit an *autosomal dominant* condition. Huntington disease, which is inherited in an autosomal dominant manner, is characterized by loss of coordination, uncontrollable dancelike movements, cognitive impairment, and personality changes, typically beginning gradually near age forty. An affected person has an affected parent. Autosomal dominant disorders tend to begin in adulthood; autosomal recessive disorders usually have an early onset.

A third major mode of inheritance is *X-linked recessive*. For a female, X-linked inheritance is like autosomal recessive inheritance, because she has two X chromosomes. That is, she can be a heterozygote or a homozygote. For a male, however, recessive alleles on the lone X chromosome are always expressed. A male with an X-linked condition inherits it from a mother who is either a carrier or affected; he does not inherit an X chromosome from his father. Colorblindness and the blood-clotting disorder hemophilia A are X-linked recessive conditions.

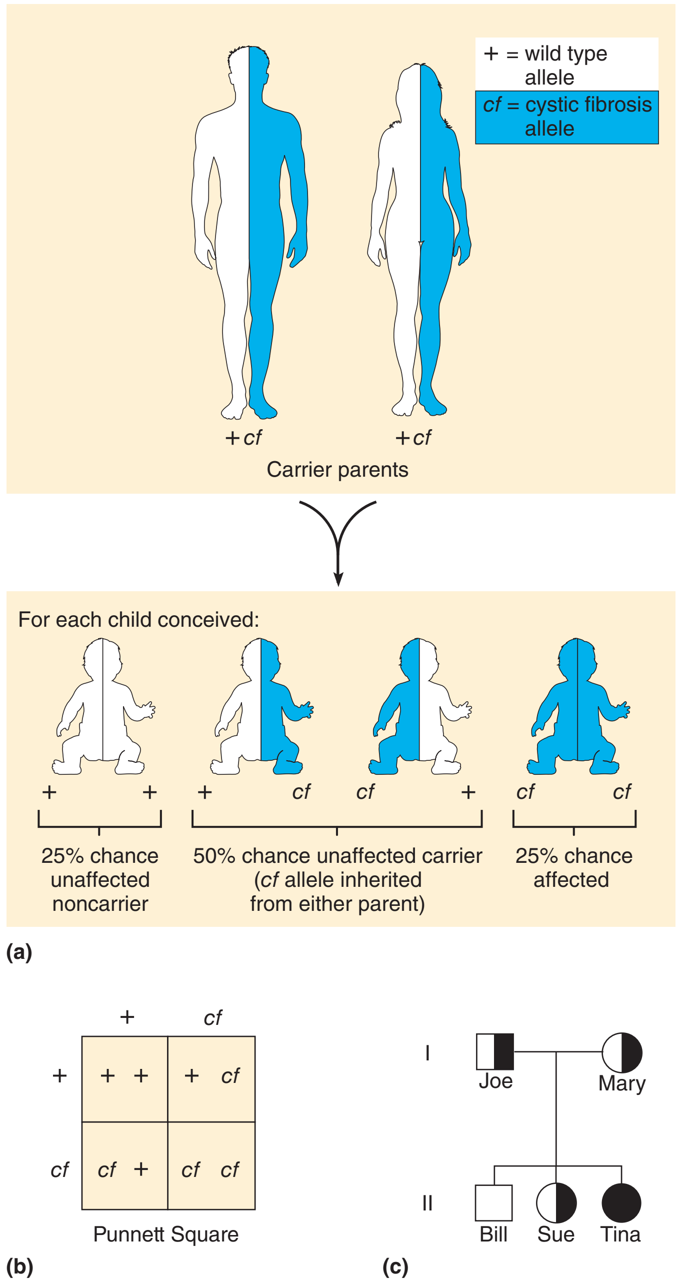

+ = wild type allele
cf = cystic fibrosis allele
+cf
+cf
Carrier parents
For each child conceived:
+ +
+ cf
cf +
cf cf
25% chance unaffected noncarrier
50% chance unaffected carrier (cf allele inherited from either parent)
25% chance affected
(a)
+
cf
+
+ +
+ cf
cf
cf +
cf cf
Punnett Square
(b)
I
Joe
Mary
II
Bill
Sue
Tina
(c)

**FIGURE 20.19** Cystic fibrosis is autosomal recessive. **(a)** Each child has a 25% chance of being unaffected and not a carrier, a 50% chance of being an unaffected carrier, and a 25% chance of being affected. Sexes are affected with equal frequency. A Punnett square **(b)** and a pedigree **(c)** are other ways of depicting this information. Symbols in the pedigree with both black and white indicate unaffected carriers (heterozygotes).

**Q** *If a female is homozygous wild type for the CFTR gene, what is the probability that her offspring will have CF?*

**Answer can be found in Appendix F on page 582.**

**PRACTICE**

38. Distinguish between dominant and recessive alleles.
39. How do Punnett squares and pedigrees depict gene transmission?
40. Compare the three modes of inheritance.

## Multifactorial Traits

Nearly all inherited traits and disorders are influenced by environmental factors, such as nutrition, physical activity, and exposure to toxins and pathogens. Genes also influence each other. Environmental influences are particularly noticeable for traits determined by more than one gene, termed *polygenic.* Usually several genes contribute, in differing degrees, toward molding the overall phenotype of a polygenic trait. Such a trait is said to be "continuously varying," which means that there are many degrees of its expression. Height, skin color, and intelligence are polygenic traits that show great variation.

When individuals with a polygenic trait are categorized into classes and the frequencies of the classes are plotted as a bar graph, a bell-shaped curve emerges. The curves are strikingly similar for different polygenic traits. Figure 20.20 vividly shows the effect of the environment in the bell curve for height—as nutrition improved during the time span between the two photos, the heights of the tallest people increased.

Traits molded by one or more genes plus the environment are termed *multifactorial,* or complex. Height and skin color are multifactorial as well as polygenic, because they are influenced by environmental factors—

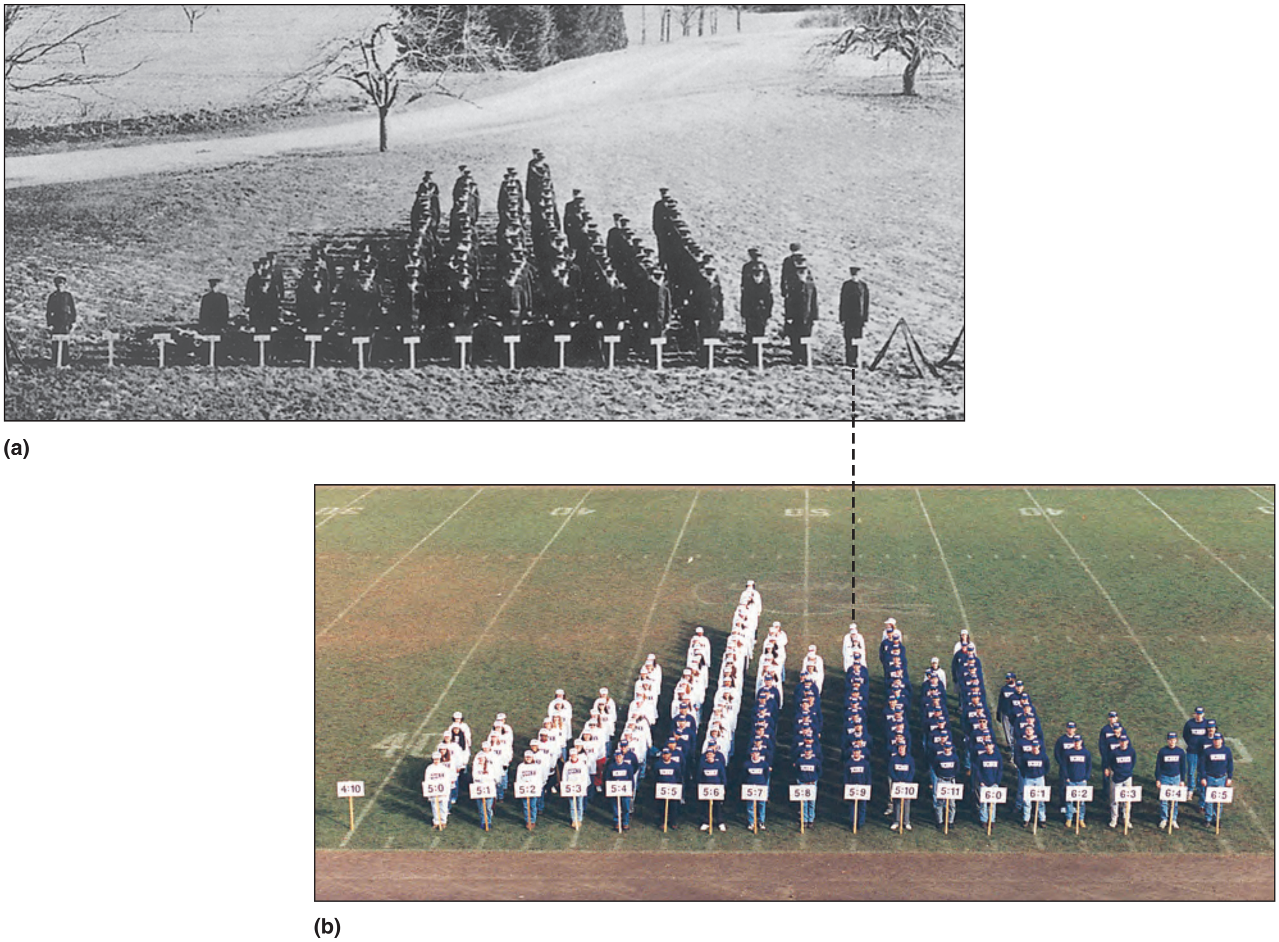


**FIGURE 20.20** Previous editions of this (and other) textbooks have used the photograph in **(a)** to illustrate the continuously varying nature of height. In the photo, taken around 1920, 175 cadets at the Connecticut Agricultural College lined up by height. In 1997, Professor Linda Strausbaugh asked her genetics students at the school, today the University of Connecticut at Storrs, to recreate the scene **(b)**. They did, and confirmed the continuously varying nature of human height. But they also demonstrated how height increased during the twentieth century, largely due to improved nutrition. The tallest people in the old photograph **(a)** are 5'9'' tall, whereas the tallest people in the more recent photograph **(b)** are 6'5'' tall.

nutrition and sun exposure, respectively. Most of the more common illnesses, including heart disease, diabetes mellitus, hypertension, and cancers, are multifactorial, as are most polygenic traits. An exception may be eye color, on which the environment has little, if any, impact.

**PRACTICE**

41. What is a polygenic trait?
42. What is a multifactorial trait?

## Summary Outline

### 20.1 Introduction (p. 550)

*Growth is an increase in size. Development is the process of changing from one life phase to another.*

### 20.2 Fertilization (p. 550)

1. Transport of sex cells
    a. A male deposits semen in the vagina during sexual intercourse.
    b. A sperm cell lashes its tail to move and is aided by muscular contractions in the female reproductive tract.
2. Sperm cell joins egg cell
    a. With the aid of enzymes, a sperm cell penetrates the corona radiata and zona pellucida.
    b. When a sperm cell head fuses with the secondary oocyte's cell membrane, changes in the membrane and the zona pellucida prevent entry of additional sperm cells.
    c. Completion of meiosis forms the second polar body.
    d. Fusion of the pronuclei from the two sex cells completes fertilization.
    e. The product of fertilization is a zygote with 46 chromosomes.

### 20.3 Pregnancy and the Prenatal Period (p. 551)

*Pregnancy is the presence of a developing offspring in the uterus. The prenatal period consists of the period of cleavage, the embryonic stage, and the fetal stage.*

1. Period of cleavage
    a. Cells undergo mitosis, giving rise to smaller and smaller cells during cleavage.
    b. The developing offspring moves down the uterine tube to the uterus, where it implants in the endometrium.
    c. The offspring is called an embryo from about the time of implantation through the eighth week of development. Thereafter it is a fetus.
    d. Eventually, embryonic and maternal cells form a placenta.
2. Hormonal changes during pregnancy
    a. Embryonic cells produce human chorionic gonadotropin (hCG), which maintains the corpus luteum.
    b. Placental tissue produces high concentrations of estrogens and progesterone.
        (1) Estrogens and progesterone maintain the uterine wall and inhibit secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH).
        (2) Progesterone and relaxin inhibit contraction of uterine muscles.
        (3) Estrogens enlarge the vagina.
        (4) Relaxin helps relax the connective tissue of the pelvic joints.
    c. Placental lactogen stimulates development of the breasts and mammary glands.
    d. During pregnancy, increased aldosterone secretion promotes retention of sodium and body fluid. Increased secretion of parathyroid hormone helps maintain a high concentration of maternal blood calcium.
3. Embryonic stage
    a. The embryonic stage extends from the beginning of the second week through the eighth week of development.
    b. During this stage, the placenta and main internal and external body structures develop.
    c. Chorionic villi develop and are surrounded by spaces filled with maternal blood.
    d. A fluid-filled amnion develops around the embryo.
    e. The embryonic disc becomes cylindrical and attaches to the developing placenta by the connecting stalk.
    f. The cells of the inner cell mass organize into primary germ layers.
    g. The yolk sac forms on the underside of the embryonic disc.
    h. The allantois extends from the yolk sac into the connecting stalk.
    i. The umbilical cord forms as the amnion envelops the tissues attached to the underside of the embryo.
    j. The placental membrane consists of the epithelium of the chorionic villi and the endothelium of the capillaries inside the villi.
        (1) Oxygen and nutrients diffuse from maternal blood across the placental membrane and into fetal blood.
        (2) Carbon dioxide and other wastes diffuse from fetal blood across the placental membrane and into maternal blood.
    k. By the beginning of the eighth week, the embryo is recognizable as human.
4. Fetal stage
    a. The fetal stage extends from the end of the eighth week of development until birth.
    b. Existing structures grow and mature. Only a few new parts appear.
    c. The fetus is full-term at the end of the ninth month.
5. Fetal blood and circulation
    a. Umbilical vessels carry blood between the placenta and the fetus.
    b. Fetal blood carries a greater concentration of oxygen than does maternal blood because the concentration of oxygen-carrying hemoglobin is greater in fetal blood, and fetal hemoglobin has greater affinity for oxygen.
    c. Blood enters the fetus through the umbilical vein and partially bypasses the liver by means of the ductus venosus.
    d. Blood enters the right atrium and partially bypasses the lungs by means of the foramen ovale.
    e. Blood entering the pulmonary trunk partially bypasses the lungs by means of the ductus arteriosus.
    f. Blood enters the umbilical arteries from the internal iliac arteries.
6. Birth process
    a. During pregnancy, placental progesterone inhibits uterine contractions.
    b. A variety of factors promote birth.
        (1) A decreasing progesterone concentration and the release of prostaglandins may initiate the birth process.
        (2) The posterior pituitary gland releases oxytocin.
        (3) Oxytocin stimulates uterine muscles to contract, and labor begins.
    c. Following birth, placental tissues are expelled.

7. Milk production and secretion
   a. Following childbirth, concentrations of placental hormones decline, the action of prolactin is no longer blocked, and the mammary glands begin to secrete milk.
   b. A reflex response to mechanical stimulation of the nipple stimulates the posterior pituitary gland to release oxytocin, which causes the alveolar ducts to eject milk.

### 20.4 Postnatal Period (p. 566)

1. Neonatal period
   a. The neonatal period extends from birth to the end of the first four weeks.
   b. The newborn must begin to respire, obtain nutrients, excrete wastes, and regulate body temperature.
   c. The first breath must be powerful to expand the lungs.
   d. The liver is immature and unable to supply sufficient glucose, so the newborn depends primarily on stored fat for energy.
   e. A newborn's immature kidneys cannot concentrate urine well.
   f. A newborn's homeostatic mechanisms may function imperfectly, and body temperature may be unstable.
   g. The cardiovascular system changes when placental circulation ceases.
      (1) Umbilical vessels constrict.
      (2) The ductus venosus constricts.
      (3) Tissue flaps close the foramen ovale as blood pressure in the right atrium falls and pressure in the left atrium rises.
      (4) The ductus arteriosus constricts.

### 20.5 Aging (p. 567)

1. Passive aging entails breakdown of structures and slowing or failure of functions.
2. Active aging involves apoptosis.

### 20.6 Genetics (p. 569)

1. Chromosomes and genes are paired
   a. Karyotypes are charts that display the two copies of each of the 22 autosomes, which do not carry genes that determine sex, and the sex chromosomes (X and Y), which do.
   b. A person with two identical variants, or alleles, for a gene is homozygous. A person with two different alleles is heterozygous.
   c. The combination of alleles is the genotype; their expression as a trait is the phenotype.
2. Modes of inheritance
   a. A dominant allele masks the expression of a recessive allele.
   b. Modes of inheritance include autosomal recessive, in which an affected individual inherits an illness from heterozygous or affected parents; autosomal dominant, in which one affected parent passes on the condition; and X-linked recessive, which affects males more than females because males lack a second X chromosome to mask disease-causing recessive alleles.
   c. Punnett squares and pedigrees depict gene transmission in families.
3. Multifactorial traits
   a. Traits determined by more than one gene are polygenic.
   b. The continuously varying nature of polygenic traits can be depicted in bell-shaped curves.
   c. One or more genes and environmental influences cause a multifactorial trait.

## CHAPTER ASSESSMENTS

### 20.1 Introduction

**1.** ____________ is an increase in the size of the individual, whereas ____________ is the continuous process by which an individual changes from one life phase to another. (p. 550)

**2.** ____________ is the period of development from fertilization to birth, whereas ____________ is the period of development from birth to death. (p. 550)

### 20.2 Fertilization

**3.** Describe how sperm cells move in the female reproductive tract. (p. 550)

**4.** Summarize the events occurring after the sperm cell head enters the oocyte's cytoplasm. (p. 551)

### 20.3 Pregnancy and the Prenatal Period

**5.** Define *pregnancy.* (p. 551)

**6.** Describe the process of cleavage. (p. 552)

**7.** Distinguish between an embryo and a fetus. (p. 553)

**8.** List hormones associated with pregnancy, and describe the function of each. (p. 556)

**9.** Distinguish between the chorion and the amnion. (pp. 556–557)

**10.** Explain the function of the amniotic fluid. (p. 557)

**11.** Ectodermal cells of the developing embryo give rise to ____________________________. (p. 557)

a. bone tissue
b. the kidneys
c. the lining of the urethra
d. the epidermis

**12.** Describe the formation of the umbilical cord. (p. 558)

**13.** Describe the composition and formation of the placenta. (p. 559)

**14.** List the function(s) of the placenta. (p. 559)

**15.** List the major changes that occur during fetal development. (pp. 560–561)

**16.** Describe a full-term fetus. (p. 561)

**17.** Trace the pathway of blood from the placenta to the fetus and back to the placenta. (pp. 561–563)

**18.** Explain positive feedback and the role of hormones in the expulsion of the fetus and the afterbirth. (pp. 564–565)

**19.** Describe milk production and secretion. (pp. 565–566)

### 20.4 Postnatal Period

**20.** Explain why a newborn's first breath must be particularly forceful. (p. 566)

**21.** Relate the difficulties of the fetus in maintaining water/electrolyte and body temperature homeostasis. (p. 566)

**22.** Describe the changes in the newborn's cardiovascular system. (pp. 566–567)

### 20.5 Aging

**23.** Discuss the signs of passive and active aging and the physiological causes of these signs. (pp. 567 and 569)

### 20.6 Genetics

**24.** Distinguish between autosomes and sex chromosomes. (p. 569)

**25.** An individual with two different alleles is ____________. (p. 569)

**26.** Match the mode of inheritance with its description. (pp. 571–572)

(1) autosomal recessive
(2) autosomal dominant
(3) X-linked recessive

A. inherited by males from carrier mothers
B. inherited from one affected parent
C. inherited from two carrier (unaffected) parents

**27.** Traits that are polygenic and affected by the environment are termed ___________. Name two such traits. (p. 573)

## INTEGRATIVE ASSESSMENTS/CRITICAL THINKING

### OUTCOMES 13.2, 13.6, 20.3, 20.4

**1.** What symptoms may appear if a newborn's ductus arteriosus fails to close?

### OUTCOMES 14.8, 20.2

**2.** Why can twins resulting from a single fertilized egg exchange blood or receive organ transplants from each other without rejection, while twins resulting from two fertilized eggs sometimes cannot?

### OUTCOMES 20.2, 20.3, 20.5

**3.** What kinds of studies and information are required to determine whether a man's exposure to a potential teratogen can cause birth defects years later? How would such analysis differ if a woman were exposed?

### OUTCOMES 20.3, 20.4

**4.** What technology would enable a fetus born in the fourth month to survive in a laboratory setting? (This is not yet possible.)

### OUTCOME 20.6

**5.** Bob and Joan know from a blood test that they are each heterozygous (carriers) for the autosomal recessive gene that causes sickle cell disease. If their first three children are healthy, what is the probability that their fourth child will have the disease?

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**Anatomy & Physiology Revealed** Go more in depth as you view animations on development from ovulation to implantation.

# APPENDIX A

## Aids to Understanding Words

**acetabul-,** vinegar cup: *acetabul*um
**adip-,** fat: *adip*ose tissue
**agglutin-,** to glue together: *agglutin*ation
**aliment-,** food: *aliment*ary canal
**allant-,** sausage: *allant*ois
**alveol-,** small cavity: *alveol*us
**an-,** without: *an*aerobic respiration
**ana-,** up: *ana*bolism
**andr-,** man: *andr*ogens
**append-,** to hang something: *append*icular
**ax-,** axis: *ax*ial skeleton, *ax*on
**bil-,** bile: *bil*irubin
**-blast,** bud: osteo*blast*
**brady-,** slow: *brady*cardia
**bronch-,** windpipe: *bronch*us
**calat-,** something inserted: inter*calat*ed disc
**calyc-,** small cup: major *calyc*es
**cardi-,** heart: peri*cardi*um
**carp-,** wrist: *carp*als
**cata-,** down: *cata*bolism
**chondr-,** cartilage: *chondr*ocyte
**chorio-,** skin: *chorio*n
**choroid,** skinlike: *choroid* plexus
**chym-,** juice: *chym*e
**-clast,** break: osteo*clast*
**cleav-,** to divide: *cleav*age
**cochlea,** snail: *cochlea*
**condyl-,** knob: *condyl*e
**corac-,** a crow's beak: *corac*oid process
**cort-,** covering: renal *cort*ex
**cran-,** helmet: *cran*ial
**cribr-,** sieve: *cribr*iform plate
**cric-,** ring: *cric*oid cartilage
**-crin,** to secrete: endo*crin*e
**crist-,** crest: *crist*a galli
**cut-,** skin: sub*cut*aneous
**cyt-,** cell: *cyt*oplasm, osteo*cyt*e
**de-,** separation from: *de*hydration
**decidu-,** falling off: *decidu*ous teeth
**dendr-,** tree: *dendr*ite
**derm-,** skin: *derm*is
**detrus-,** to force away: *detrus*or muscle
**di-,** two: *di*saccharide
**diastol-,** dilation: *diastol*ic pressure
**diuret-,** to pass urine: *diuret*ic
**dors-,** back: *dors*al
**ejacul-,** to shoot forth: *ejacul*ation
**embol-,** stopper: *embol*us
**endo-,** within: *endo*plasmic reticulum, *endo*crine gland
**epi-,** upon: *epi*thelial tissue, *epi*dermis, *epi*glottis
**erg-,** work: syn*erg*ist
**erythr-,** red: *erythr*ocyte
**exo-,** outside: *exo*crine gland
**extra-,** outside: *extra*cellular fluid
**fimb-,** fringe: *fimb*riae
**follic-,** small bag: hair *follic*le, ovarian *follic*le
**fov-,** pit: *fov*ea capitis
**funi-,** small cord or fiber: *funi*culus
**gangli-,** a swelling: *gangli*on
**gastr-,** stomach: *gastr*ic gland
**-gen,** to be produced: aller*gen*
**-genesis,** origin: spermato*genesis*
**glen-,** joint socket: *glen*oid cavity
**-glia,** glue: neuro*glia*
**glom-,** little ball: *glom*erulus
**glyc-,** sweet: *glyc*ogen
**-gram,** something written: electrocardio*gram*
**hema-,** blood: *hema*tocrit
**hemo-,** blood: *hemo*globin
**hepat-,** liver: *hepat*ic duct
**hetero-,** other, different: *hetero*zygous
**hom-,** same, common: *hom*ozygous
**homeo-,** same: *homeo*stasis
**humor-,** fluid: *humor*al immunity
**hyper-,** above, more, over: *hyper*tonic, *hyper*trophy, *hyper*thyroidism
**hypo-,** below: *hypo*tonic, *hypo*thyroidism
**im-,** not: *im*balance
**immun-,** free: *immun*ity
**inflamm-,** set on fire: *inflamm*ation
**inter-,** among, between: *inter*phase, *inter*calated disc, *inter*vertebral disc
**intra-,** inside, within: *intra*membranous bone, *intra*cellular fluid
**iris,** rainbow: *iris*
**iso-,** equal: *iso*tonic
**kerat-,** horn: *kerat*in
**labi-,** lip: *labi*a minora
**labyrinth,** maze: *labyrinth*
**lacri-,** tears: *lacri*mal gland
**lacun-,** pool: *lacun*a
**laten-,** hidden: *laten*t period
**-lemm,** rind or peel: neuri*lemm*a
**leuko-,** white: *leuko*cyte
**lingu-,** tongue: *lingu*al tonsil
**lip-,** fat: *lip*ids
**-logy,** study of: physio*logy*
**-lyt,** dissolvable: electro*lyt*e
**macr-,** large: *macr*ophage
**macula,** spot: *macula* lutea
**meat-,** passage: auditory *meat*us
**melan-,** black: *melan*in
**mening-,** membrane: *mening*es
**mens-,** month: *mens*es
**meta-,** change: *meta*bolism
**mict-,** to pass urine: *mict*urition
**mit-,** thread: *mit*osis
**mono-,** one: *mono*saccharide
**mons-,** mountain: *mons* pubis
**morul-,** mulberry: *morul*a
**moto-,** moving: *motor* neuron
**mut-,** change: *mut*ation
**myo-,** muscle: *myo*fibril
**nat-,** to be born: pre*nat*al
**nephr-,** pertaining to the kidney: *nephr*on
**neutr-,** neither one nor the other: *neutr*al
**nod-,** knot: *nod*ule
**nutri-,** nourish: *nutri*ent
**odont-,** tooth: *odont*oid process
**olfact-,** to smell: *olfact*ory
**-osis,** abnormal condition: leukocyt*osis*
**os-,** bone: *os*seous tissue
**papill-,** nipple: *papill*ary muscle, renal *papill*ae
**para-,** beside: *para*thyroid glands
**pariet-,** wall: *pariet*al membrane
**path-,** disease: *path*ogen
**pelv-,** basin: *pelv*ic cavity
**peri-,** around: *peri*cardial membrane, *peri*pheral nervous system, *peri*stalsis
**phag-,** to eat: *phag*ocytosis
**pino-,** to drink: *pino*cytosis
**pleur-,** rib: *pleur*al membrane
**plex-,** interweaving: choroid *plex*us
**-poie,** make, produce: hemato*poie*sis, erythro*poie*tin
**poly-,** many: *poly*unsaturated
**pseud-,** false: *pseud*ostratified epithelium
**puber-,** adult: *puber*ty
**pyl-,** gatekeeper: *pyl*oric sphincter
**sacchar-,** sugar: mono*sacchar*ide
**sarco-,** flesh: *sarco*plasm
**scler-,** hard: *scler*a
**seb-,** grease: *seb*aceous gland
**sens-,** feeling: *sens*ory neuron
**-som,** body: ribo*som*e
**squam-,** scale: *squam*ous epithelium
**-stasis,** standing still, halt: homeo*stasis*, hemo*stasis*
**strat-,** layer: *strat*ified
**syn-,** together: *syn*thesis, *syn*ergist, *syn*apse, *syn*cytium
**systol-,** contraction: *systol*ic pressure
**tachy-,** rapid: *tachy*cardia
**tetan-,** stiff: *tetan*ic contraction
**thromb-,** clot: *thromb*ocyte
**toc-,** birth: oxy*toc*in
**-tomy,** cutting: ana*tomy*
**trigon-,** triangle: *trigon*e
**-troph-,** well fed: muscular hyper*troph*y, *troph*oblast
**-tropic,** influencing: adrenocortico*tropic*
**tympan-,** drum: *tympan*ic membrane
**umbil-,** navel: *umbil*ical cord
**ventr-,** belly or stomach: *ventr*icle
**vill-,** hairy: *villi*
**vitre-,** glass: *vitre*ous humor
**-zym,** ferment: en*zym*e

# APPENDIX B

# Scientific Method

Our knowledge of how the human body works is based on centuries of careful observation and experimentation. A way of thinking and organizing information, called the **scientific method**, guides the acquisition and interpretation of new information about the human body. The scientific method is used to either support or challenge a scientific theory, which is a systematically organized body of knowledge that applies to a variety of situations. It is a key part of a general process known as *scientific inquiry*, which includes other ways of investigating the natural world. The scientific method is a framework in which to consider ideas and evidence that involves use of familiar skills of observing, questioning, reasoning, predicting, testing, interpreting, and concluding.

The scientific method provides a sequence of logical steps that address a specific question. A proposed answer to the question is stated as a *hypothesis*, or "educated guess." More than a question or hunch, a hypothesis is based on existing knowledge and is often phrased in the form "if this is true, then that must follow." It is specific and testable, and should examine only one changeable factor, or *variable*. Even though the hypothesis may seem attractive and may make sense, it is not accepted until sufficient experimental evidence supports it. Indeed, it may be proven wrong. Experimental findings that go against the hypothesis are just as important as those that support it.

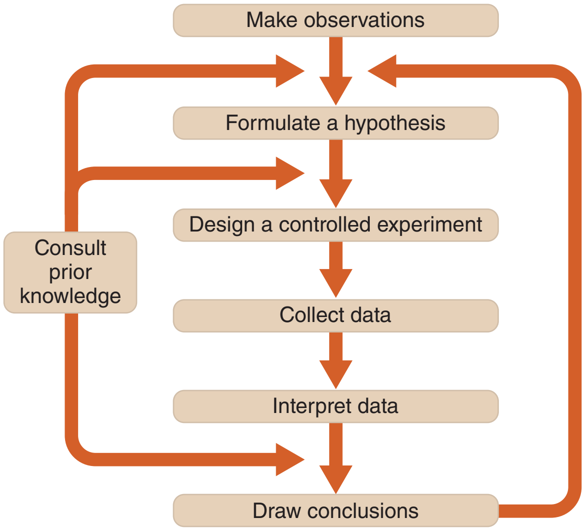
The process of drug development illustrates the use of the scientific method in anatomy and physiology. Consider a hypothesis to test a new cancer treatment:

> *If a drug blocks the receptor proteins to which a growth factor binds on cancer cells, then the cells may stop dividing and halt progression of the cancer.*

This hypothesis is based on past experiments that identified the specific receptors and growth factors that fuel a particular type of cancer and described how they interact, and observations that the cells of certain cancers have excess growth factor receptors compared to healthy cells. Using that knowledge and the hypothesis, researchers design an experiment (clinical trial), which is a test that yields information:

> *One group of patients receives the experimental treatment (new drug) and a second group (the control) receives an existing treatment.*

Experiments are carefully planned to make the results as meaningful as possible. In drug development, the control group provides a point of comparison for the new treatment, because the participants are selected to be as alike as possible. In this way, differences due to the drug can stand out. Studies should also be "double blinded" whenever possible, which means that neither participants nor researchers know which patients receive which treatment until the end of the study. Outcomes are specific. At the end of six months, if significantly more of the patients taking the experimental drug show measurable signs of improvement compared to the control group, then further study is warranted. Repeating scientific findings is essential to confirming experimental results. Before a new drug is prescribed for patients, it is tested on thousands of individuals in multiple clinical trials.



The scientific method is not a linear process, but a cycle, because results and conclusions often suggest new questions to explore. Something about the new cancer drug, for example, may suggest how it could be "repurposed" to treat a different condition. Testing begins anew.

In scientific investigations, so-called "negative" results are just as important as results that support the hypothesis. If the drug being tested doesn't work, researchers can either modify the hypothesis (perhaps the drug only works on certain subtypes of the disease) or develop more effective versions of the drug. Medical journals provide diverse examples of how the scientific method lies behind the drugs and procedures that have vastly improved the lives of many of us.

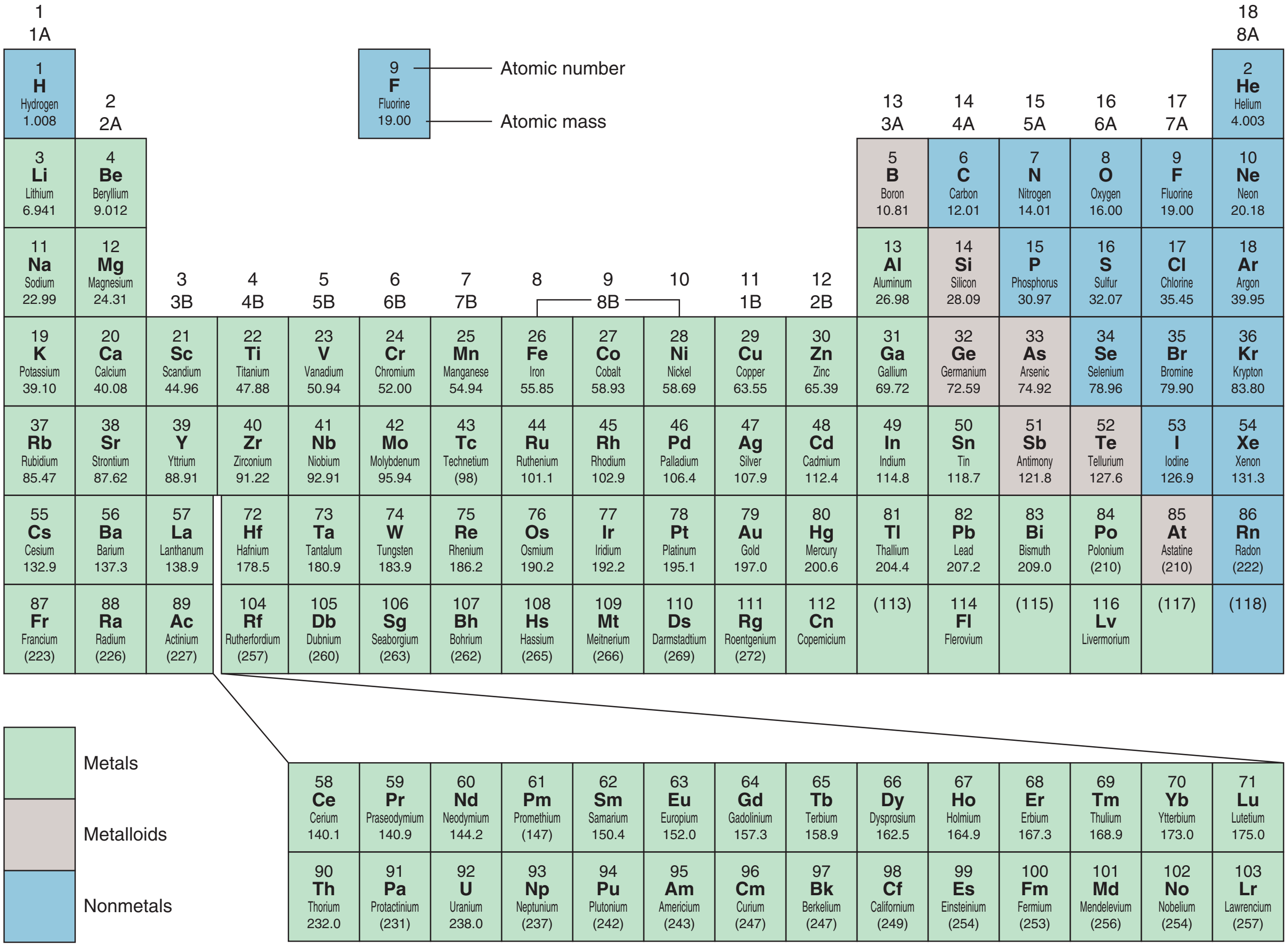
# APPENDIX C

## Metric Measurement System and Conversions

| **Measurement** | **Unit & Abbreviation** | **Metric Equivalent** | **Conversion Factor Metric to English (approximate)** | **Conversion Factor English to Metric (approximate)** |
|---|---|---|---|---|
| Length | 1 kilometer (km) | 1,000 ($10^3$) m | 1 km = 0.62 mile | 1 mile = 1.61 km |
| | 1 meter (m) | 100 ($10^2$) cm<br>1,000 ($10^3$) mm | 1 m = 1.1 yards<br>= 3.3 feet<br>= 39.4 inches | 1 yard = 0.9 m<br>1 foot = 0.3 m |
| | 1 decimeter (dm) | 0.1 ($10^{-1}$) m | 1 dm = 3.94 inches | 1 inch = 0.25 dm |
| | 1 centimeter (cm) | 0.01 ($10^{-2}$) m | 1 cm = 0.4 inches | 1 foot = 30.5 cm<br>1 inch = 2.54 cm |
| | 1 millimeter (mm) | 0.001 ($10^{-3}$) m<br>0.1 ($10^{-1}$) cm | 1 mm = 0.04 inches | |
| | 1 micrometer (µm) | 0.000001 ($10^{-6}$) m<br>0.001 ($10^{-3}$) mm | | |
| Mass | 1 metric ton (t) | 1,000 ($10^3$) kg | 1 t = 1.1 ton | 1 ton = 0.91 t |
| | 1 kilogram (kg) | 1,000 ($10^3$) g | 1 kg = 2.2 pounds | 1 pound = 0.45 kg |
| | 1 gram (g) | 1,000 ($10^3$) mg | 1 g = 0.04 ounce | 1 pound = 454 g<br>1 ounce = 28.35 g |
| | 1 milligram (mg) | 0.001 ($10^{-3}$) g | | |
| | 1 microgram (µg) | 0.000001 ($10^{-6}$) g | | |
| Volume (liquids and gases) | 1 liter (L) | 1,000 ($10^3$) mL | 1 L = 1.06 quarts | 1 gallon = 3.78 L<br>1 quart = 0.95 L |
| | 1 milliliter (mL) | 0.001 ($10^{-3}$) L<br>1 cubic centimeter (cc or $cm^3$) | 1 mL = 0.03 fluid ounce<br>1 mL = 1/5 teaspoon<br>1 mL = 15–16 drops | 1 quart = 946 mL<br>1 fluid ounce = 29.6 mL<br>1 teaspoon = 5 mL |
| Time | 1 second (s) | 1/60 minute | same | same |
| | 1 millisecond (ms) | 0.001 ($10^{-3}$) s | same | same |
| Temperature | Degrees Celsius (°C) | | °F = 9/5°C + 32 | °C = 5/9 (°F – 32) |

# APPENDIX D

## Periodic Table of the Elements



9
F
Fluorine
19.00

Atomic number
Atomic mass

| 1<br>1A | 2<br>2A | 3<br>3B | 4<br>4B | 5<br>5B | 6<br>6B | 7<br>7B | 8 | 9<br>8B | 10 | 11<br>1B | 12<br>2B | 13<br>3A | 14<br>4A | 15<br>5A | 16<br>6A | 17<br>7A | 18<br>8A |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1<br>**H**<br>Hydrogen<br>1.008 | | | | | | | | | | | | | | | | | 2<br>**He**<br>Helium<br>4.003 |
| 3<br>**Li**<br>Lithium<br>6.941 | 4<br>**Be**<br>Beryllium<br>9.012 | | | | | | | | | | | 5<br>**B**<br>Boron<br>10.81 | 6<br>**C**<br>Carbon<br>12.01 | 7<br>**N**<br>Nitrogen<br>14.01 | 8<br>**O**<br>Oxygen<br>16.00 | 9<br>**F**<br>Fluorine<br>19.00 | 10<br>**Ne**<br>Neon<br>20.18 |
| 11<br>**Na**<br>Sodium<br>22.99 | 12<br>**Mg**<br>Magnesium<br>24.31 | | | | | | | | | | | 13<br>**Al**<br>Aluminum<br>26.98 | 14<br>**Si**<br>Silicon<br>28.09 | 15<br>**P**<br>Phosphorus<br>30.97 | 16<br>**S**<br>Sulfur<br>32.07 | 17<br>**Cl**<br>Chlorine<br>35.45 | 18<br>**Ar**<br>Argon<br>39.95 |
| 19<br>**K**<br>Potassium<br>39.10 | 20<br>**Ca**<br>Calcium<br>40.08 | 21<br>**Sc**<br>Scandium<br>44.96 | 22<br>**Ti**<br>Titanium<br>47.88 | 23<br>**V**<br>Vanadium<br>50.94 | 24<br>**Cr**<br>Chromium<br>52.00 | 25<br>**Mn**<br>Manganese<br>54.94 | 26<br>**Fe**<br>Iron<br>55.85 | 27<br>**Co**<br>Cobalt<br>58.93 | 28<br>**Ni**<br>Nickel<br>58.69 | 29<br>**Cu**<br>Copper<br>63.55 | 30<br>**Zn**<br>Zinc<br>65.39 | 31<br>**Ga**<br>Gallium<br>69.72 | 32<br>**Ge**<br>Germanium<br>72.59 | 33<br>**As**<br>Arsenic<br>74.92 | 34<br>**Se**<br>Selenium<br>78.96 | 35<br>**Br**<br>Bromine<br>79.90 | 36<br>**Kr**<br>Krypton<br>83.80 |
| 37<br>**Rb**<br>Rubidium<br>85.47 | 38<br>**Sr**<br>Strontium<br>87.62 | 39<br>**Y**<br>Yttrium<br>88.91 | 40<br>**Zr**<br>Zirconium<br>91.22 | 41<br>**Nb**<br>Niobium<br>92.91 | 42<br>**Mo**<br>Molybdenum<br>95.94 | 43<br>**Tc**<br>Technetium<br>(98) | 44<br>**Ru**<br>Ruthenium<br>101.1 | 45<br>**Rh**<br>Rhodium<br>102.9 | 46<br>**Pd**<br>Palladium<br>106.4 | 47<br>**Ag**<br>Silver<br>107.9 | 48<br>**Cd**<br>Cadmium<br>112.4 | 49<br>**In**<br>Indium<br>114.8 | 50<br>**Sn**<br>Tin<br>118.7 | 51<br>**Sb**<br>Antimony<br>121.8 | 52<br>**Te**<br>Tellurium<br>127.6 | 53<br>**I**<br>Iodine<br>126.9 | 54<br>**Xe**<br>Xenon<br>131.3 |
| 55<br>**Cs**<br>Cesium<br>132.9 | 56<br>**Ba**<br>Barium<br>137.3 | 57<br>**La**<br>Lanthanum<br>138.9 | 72<br>**Hf**<br>Hafnium<br>178.5 | 73<br>**Ta**<br>Tantalum<br>180.9 | 74<br>**W**<br>Tungsten<br>183.9 | 75<br>**Re**<br>Rhenium<br>186.2 | 76<br>**Os**<br>Osmium<br>190.2 | 77<br>**Ir**<br>Iridium<br>192.2 | 78<br>**Pt**<br>Platinum<br>195.1 | 79<br>**Au**<br>Gold<br>197.0 | 80<br>**Hg**<br>Mercury<br>200.6 | 81<br>**Tl**<br>Thallium<br>204.4 | 82<br>**Pb**<br>Lead<br>207.2 | 83<br>**Bi**<br>Bismuth<br>209.0 | 84<br>**Po**<br>Polonium<br>(210) | 85<br>**At**<br>Astatine<br>(210) | 86<br>**Rn**<br>Radon<br>(222) |
| 87<br>**Fr**<br>Francium<br>(223) | 88<br>**Ra**<br>Radium<br>(226) | 89<br>**Ac**<br>Actinium<br>(227) | 104<br>**Rf**<br>Rutherfordium<br>(257) | 105<br>**Db**<br>Dubnium<br>(260) | 106<br>**Sg**<br>Seaborgium<br>(263) | 107<br>**Bh**<br>Bohrium<br>(262) | 108<br>**Hs**<br>Hassium<br>(265) | 109<br>**Mt**<br>Meitnerium<br>(266) | 110<br>**Ds**<br>Darmstadtium<br>(269) | 111<br>**Rg**<br>Roentgenium<br>(272) | 112<br>**Cn**<br>Copernicium | (113) | 114<br>**Fl**<br>Flerovium | (115) | 116<br>**Lv**<br>Livermorium | (117) | (118) |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 58<br>**Ce**<br>Cerium<br>140.1 | 59<br>**Pr**<br>Praseodymium<br>140.9 | 60<br>**Nd**<br>Neodymium<br>144.2 | 61<br>**Pm**<br>Promethium<br>(147) | 62<br>**Sm**<br>Samarium<br>150.4 | 63<br>**Eu**<br>Europium<br>152.0 | 64<br>**Gd**<br>Gadolinium<br>157.3 | 65<br>**Tb**<br>Terbium<br>158.9 | 66<br>**Dy**<br>Dysprosium<br>162.5 | 67<br>**Ho**<br>Holmium<br>164.9 | 68<br>**Er**<br>Erbium<br>167.3 | 69<br>**Tm**<br>Thulium<br>168.9 | 70<br>**Yb**<br>Ytterbium<br>173.0 | 71<br>**Lu**<br>Lutetium<br>175.0 |
| 90<br>**Th**<br>Thorium<br>232.0 | 91<br>**Pa**<br>Protactinium<br>(231) | 92<br>**U**<br>Uranium<br>238.0 | 93<br>**Np**<br>Neptunium<br>(237) | 94<br>**Pu**<br>Plutonium<br>(242) | 95<br>**Am**<br>Americium<br>(243) | 96<br>**Cm**<br>Curium<br>(247) | 97<br>**Bk**<br>Berkelium<br>(247) | 98<br>**Cf**<br>Californium<br>(249) | 99<br>**Es**<br>Einsteinium<br>(254) | 100<br>**Fm**<br>Fermium<br>(253) | 101<br>**Md**<br>Mendelevium<br>(256) | 102<br>**No**<br>Nobelium<br>(254) | 103<br>**Lr**<br>Lawrencium<br>(257) |

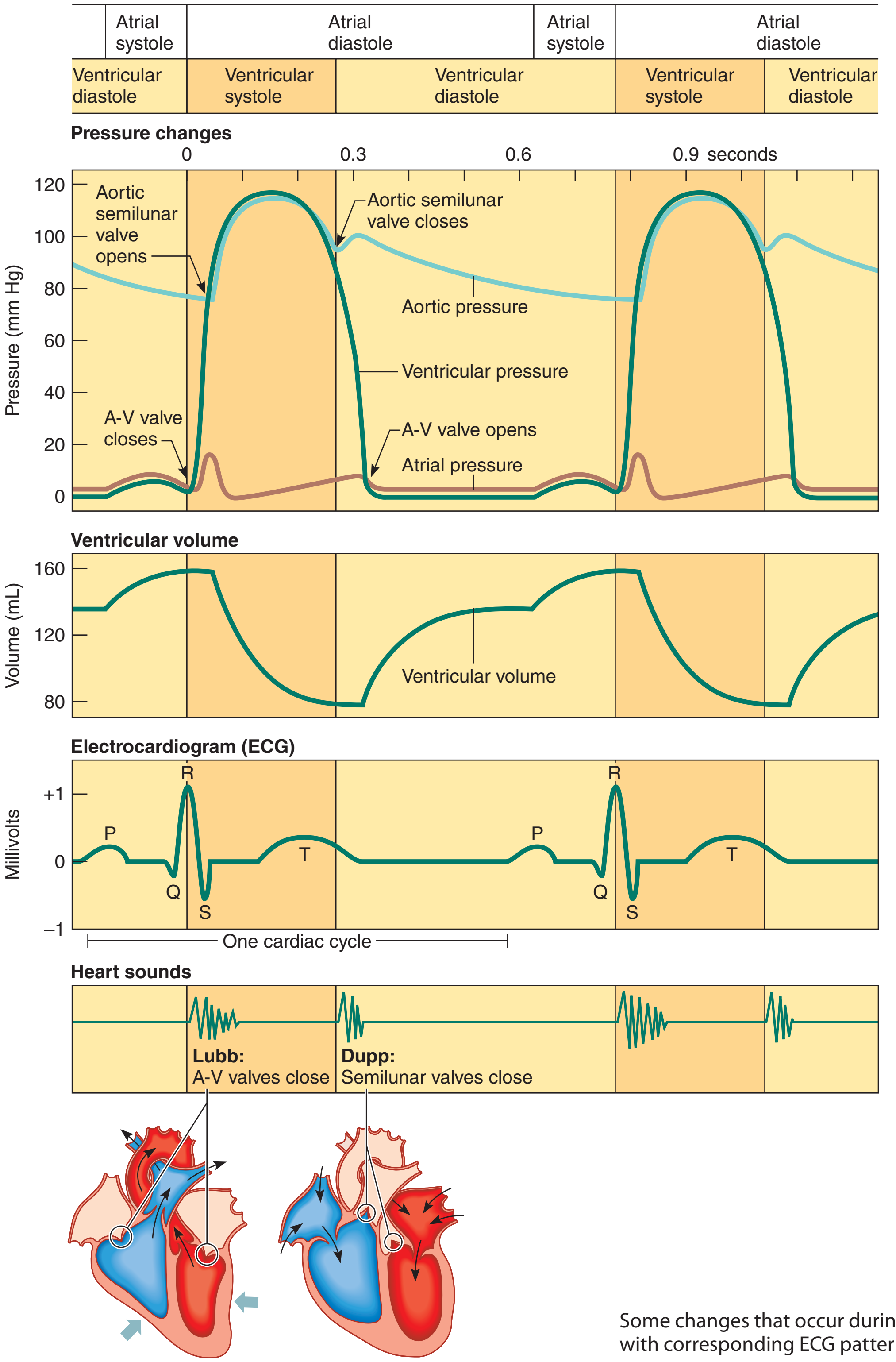
🟩 Metals
▨ Metalloids
🟦 Nonmetals

The 1–18 group designation has been recommended by the International Union of Pure and Applied Chemistry (IUPAC) but is not yet in wide use.

Elements up to 122 have been reported. Of these, some of the higher-numbered elements have only been observed under laboratory conditions, and have not been confirmed.

# APPENDIX E

## Changes During the Cardiac Cycle


Atrial systole
Atrial diastole
Atrial systole
Atrial diastole
Ventricular diastole
Ventricular systole
Ventricular diastole
Ventricular systole
Ventricular diastole
Pressure changes
0
0.3
0.6
0.9 seconds
Pressure (mm Hg)
120
100
80
60
40
20
0
Aortic semilunar valve opens
Aortic semilunar valve closes
Aortic pressure
Ventricular pressure
A-V valve closes
A-V valve opens
Atrial pressure
Ventricular volume
Volume (mL)
160
120
80
Ventricular volume
Electrocardiogram (ECG)
Millivolts
+1
0
–1
P
R
Q
S
T
P
R
Q
S
T
One cardiac cycle
Heart sounds
Lubb:
A-V valves close
Dupp:
Semilunar valves close

Some changes that occur during the cardiac cycle, with corresponding ECG pattern and heart sounds.

# APPENDIX F

# Figure Question Answers

### *Chapter 1*

**Figure 1.6:** The heat would come on until the temperature reached the new set point.
**Figure 1.14:** The hand is more lateral than the hip (remember that anatomical position is the reference).

### *Chapter 2*

**Figure 2.11:** pH 7.4, the same as the pH of human blood
**Figure 2.14:** Fats are a subgroup of lipids. Other lipids include the steroids and the phospholipids.

### *Chapter 3*

**Figure 3.10:** chromatin and nucleolus
**Figure 3.18:** a carrier protein and cellular energy

### *Chapter 4*

**Figure 4.9:** cytosol
**Figure 4.13:** messenger RNA

### *Chapter 5*

**Figure 5.8:** cross section, although the lumen is not circular and has an irregular shape
**Figure 5.21:** fluid

### *Chapter 6*

**Figure 6.2:** palms of hands, soles of feet
**Figure 6.4:** lunula

### *Chapter 7*

**Figure 7.8:** receptors, control center (set point), effectors
**Figure 7.29:** Female obturator foramen is more triangular, male is more oval. Female pubic arch is a wider (greater) angle than the male pubic arch. Female ilia are more flared than those on the male hip bones.

### *Chapter 8*

**Figure 8.5:** by diffusion
**Figure 8.8:** their lengths stay the same

### *Chapter 9*

**Figure 9.12:** ATP
**Figure 9.33:** inferior

### *Chapter 10*

**Figure 10.6:** temporal bone
**Figure 10.16:** Yes, voluntary control–look up at the ceiling if you have a question about this!

### *Chapter 11*

**Figure 11.1:** specific receptors
**Figure 11.15:** exocrine

### *Chapter 12*

**Figure 12.12:** macrophage
**Figure 12.16:** the conversion of soluble fibrinogen to insoluble fibrin

### *Chapter 13*

**Figure 13.14:** ventricular depolarization and atrial repolarization
**Figure 13.21:** impermeant solute, plasma proteins
**Figure 13.30:** radial artery and ulnar artery
**Figure 13.33:** axillary vein

### *Chapter 14*

**Figure 14.4:** thoracic duct
**Figure 14.17:** secondary immune response

### *Chapter15*

**Figure 15.2:** 127 inches or 10.6 feet
**Figure 15.19.** The pancreas is stimulated to secrete digestive enzymes.
**Figure 15.30:** The major secretion from these cells in the large intestinal wall is mucus to protect against the abrasiveness of material flowing through the tube, to bind fecal matter, and to control pH of the large intestinal contents.

### *Chapter 16*

**Figure 16.8:** because it carries oxygen-poor blood
**Figure 16.15:** upward

### *Chapter 17*

**Figure 17.10:** afferent arteriole
**Figure 17.13:** tubular reabsorption

### *Chapter 18*

**Figure 18.2:** potassium
**Figure 18.8:** Exhalation excretes $CO_2$. $CO_2$ excretion controls the amount of $CO_2$ in the blood. If blood $CO_2$ is too high (not enough excreted), excess carbonic acid is formed and pH drops. If blood $CO_2$ is too low (too much excreted), pH rises. Control of $CO_2$ excretion keeps blood pH constant at 7.4.

### *Chapter19*

**Figure 19.3:** Normally the sperm and egg each have 23 chromosomes, so that upon fertilization, the developing zygote will have the full complement of 46 chromosomes in human cells.
**Figure 19.10:** corona radiata
**Figure 19.16:** oral contraceptives

### *Chapter 20*

**Figure 20.2:** 23 chromosomes, each with 2 chromatids
**Figure 20.14:** umbilical vein, umbilical arteries, ductus venosus, ductus arteriosus, foramen ovale
**Figure 20.19:** zero chance of having the disease (CF, cystic fibrosis)

# GLOSSARY

A phonetic guide to pronunciation follows each glossary word. Any unmarked vowel that ends a syllable or stands alone as a syllable has the long sound. Thus, the word *play* is phonetically spelled *pla*. Any unmarked vowel followed by a consonant has the short sound. The word *tough*, for instance, is phonetically spelled *tuf*. If a long vowel appears in the middle of a syllable (followed by a consonant), it is marked with a macron (¯), the sign for a long vowel. Thus, the word plate is phonetically spelled *plāt*. Similarly, if a vowel stands alone or ends a syllable, but has a short sound, it is marked with a breve (˘).

## A

**abdominal cavity** (ab-dom′ĭ-nal kav′ĭ-te) Space between the diaphragm and the pelvic inlet that contains the abdominal viscera.

**abdominopelvic cavity** (ab-dom″ĭ-no-pel′vik kav′ĭ-te) Space between the diaphragm and the pelvic outlet that contains the abdominal and pelvic viscera.

**abduction** (ab-duk′shun) Movement of a body part away from the midline.

**accessory organ** (ak-ses′o-re or′gan) Organ that supplements the functions of other organs.

**accommodation** (ah-kom″o-da′shun) Adjustment of the lens of the eye for close or distant vision.

**acetylcholine** (as″ĕ-til-ko′lēn) **(ACH)** Type of neurotransmitter, which is a biochemical secreted into the synaptic cleft at axon ends of neurons.

**acetylcholinesterase** (as″ĕ-til-ko″lin-es′ter-ās) Enzyme that catalyzes breakdown of acetylcholine.

**acid** (as′id) Substance that ionizes in water to release hydrogen ions.

**acidosis** (as″ĭ-do′sis) Decrease in pH of body fluids below pH 7.35.

**ACTH** Adrenocorticotropic hormone.

**actin** (ak′tin) Protein in a muscle fiber that forms filaments that slide between filaments of the protein myosin, contracting muscle fibers.

**action potential** (ak′shun po-ten′shal) Sequence of electrical changes in part of a nerve cell or muscle cell exposed to a stimulus that exceeds threshold.

**active site** (ak′tiv sīt) Part of an enzyme molecule that temporarily binds a substrate.

**active transport** (ak′tiv trans′port) Process that requires energy and a carrier molecule to move a substance across a cell membrane against the concentration gradient.

**adaptation** (ad″ap-tā′shun) Ability of the nervous system to become less responsive to a sustained stimulus.

**adaptive defense** (a-dap′tiv dē-fenc) Specific defenses T and B cells carry out.

**adduction** (ah-duk′shun) Movement of body part toward the midline.

**adenosine triphosphate** (ah-den′o-sēn tri-fos′fāt) **(ATP)** Organic molecule that transfers energy, used in cellular processes.

**ADH** Antidiuretic hormone.

**adipose tissue** (ad′ĭ-pōs tish′u) Fat-storing tissue.

**adrenal cortex** (ah-dre′nal kor′teks) Outer part of the adrenal gland.

**adrenal gland** (ah-dre′nal gland) Endocrine gland on the superior portion of each kidney.

**adrenal medulla** (ah-dre′nal me-dul′ah) Inner part of the adrenal gland.

**adrenergic fiber** (ad″ren-er′jik fi′ber) Axon that secretes norepinephrine at its terminal.

**adrenocorticotropic hormone** (ad-re″no-kor″te-ko-trōp′ik hor′mōn) **(ACTH)** Hormone that the anterior pituitary secretes to stimulate activity in the adrenal cortex.

**aerobic respiration** (a″er-o′bik res″pĭ-ra′shun) Complete, energy-releasing, breakdown of glucose to carbon dioxide and water in the presence of oxygen.

**afferent arteriole** (af′er-ent ar-te′re-ōl) Vessel that conveys blood to the glomerulus of each kidney nephron.

**agglutination** (ah-gloo″tĭ-na′shun) Clumping of blood cells in response to a reaction between an antibody and an antigen.

**agonist** (ago′-nist) A muscle that causes a movement

**agranulocyte** (a-gran′u-lo-sīt) Nongranular leukocyte.

**albumin** (al-bu′min) Plasma protein that helps regulate the colloid osmotic pressure of blood.

**aldosterone** (al-dos′ter-ōn″) Adrenal cortical hormone that regulates sodium and potassium ion concentrations and fluid volume.

**alimentary canal** (al″i-men′tar-e kah-nal′) Tubular part of the digestive tract from the mouth to the anus.

**alkalosis** (al″kah-lo′sis) Increase in pH of body fluids above pH 7.45.

**allantois** (ah-lan′to-is) Structure in the embryo from which the umbilical cord blood vessels develop.

**allele** (ah-le′el) One of two or more forms of a gene.

**allergen** (al′er-jen) Chemical that triggers the immune response.

**alveolar duct** (al-ve′o-lar dukt) Fine tube that conducts inhaled air to an air sac of the lungs.

**alveolus** (al-ve′o-lus) (plural, *alveoli*) Air sac of a lung; a saclike structure.

**amino acid** (ah-me′no as′id) Organic compound that includes an amino group ($-NH_2$) and a carboxyl group ($-COOH$); the structural unit of a protein molecule.

**amnion** (am′ne-on) Extraembryonic membrane that encircles a fetus and contains amniotic fluid.

**amniotic fluid** (am″ne-ot′ik floo′id) Fluid in the amniotic cavity that surrounds the developing fetus.

**ampulla** (am-pul′ah) Expansion at the end of each semicircular canal that houses a crista ampullaris.

**anabolism** (ah-nab′o-lizm) Synthesis of larger molecules from smaller ones; anabolic metabolism.

**anaerobic respiration** (an″er-o′bik res″pĭ-ra′shun) Energy-releasing reactions that occur in the absence of molecular oxygen.

**anaphase** (an′ah-fāz) Stage in mitosis when replicated chromosomes separate and move to opposite poles of the cell.

**anatomy** (ah-nat′o-me) Branch of science dealing with the form and structure of body parts.

**androgen** (an′dro-jen) Male sex hormone such as testosterone.

**antagonist** (an-tag′o-nist) Muscle that opposes an agonist.

**antebrachial** (an″te-bra′ke-al) Pertaining to the forearm.

**antecubital** (an″te-ku′bĭ-tal) Region anterior to the elbow joint.

**anterior** (an-te′re-or) Pertaining to the front.

**anterior pituitary** (an-te′re-or pĭ-tu′ĭ-tār″e) Front lobe of the pituitary gland.

**antibody** (an′tĭ-bod″e) Protein that B cells of the immune system produce in response to a nonself antigen; it reacts with the antigen; immunoglobulin.

**anticodon** (an″tĭ-ko′don) Three nucleotides of a transfer RNA molecule that are complementary to a specific mRNA codon.

**antidiuretic hormone** (an″tĭ-di″u-ret′ik hor′mōn) **(ADH)** Hormone of the posterior pituitary gland that enhances water conservation in the kidneys.

**antigen** (an′tĭ-jen) Chemical that triggers an immune response.

**aorta** (a-or′tah) Major systemic artery that receives blood directly from the left ventricle.

**aortic sinus** (a-or′tik si′nus) Swelling in the aortic wall, behind each cusp of the semilunar valve, that contains baroreceptors.

**aortic valve** (a-or′tik valv) Flaplike structures in the wall of the aorta near its origin that prevent blood from returning to the left ventricle of the heart.

**apocrine gland** (ap′o-krin gland) Type of gland whose secretions have parts of secretory cells.

**aponeurosis** (ap″o-nu-ro′sis) Sheet of connective tissue that attaches muscles to muscles.

**apoptosis** (ayp-o-toe′sis) Programmed cell death.

**appendicular** (ap″en-dik′u-lar) Pertaining to the upper or lower limbs.

**aqueous humor** (a′kwe-us hu′mor) Watery fluid that fills the anterior cavity of the eye.

**arachnoid mater** (ah-rak′noid ma′ter) Delicate, weblike middle layer of meninges.

**areolar tissue** (ah-re′o-lar tish′u) Connective tissue composed mainly of fibers.

**arrector pili muscle** (ah-rek′tor pil′i mus′l) Smooth muscle in the skin associated with a hair follicle.

**arteriole** (ar-te′re-ōl) Small branch of an artery that communicates with a capillary network.

**artery** (ar′ter-e) Vessel that transports blood from the heart.

**articular cartilage** (ar-tik′u-lar kar′tĭ-lij) Hyaline cartilage that covers the ends of bones in synovial joints.

**ascending tract** (ah-send′ing trakt) Group of nerve fibers in the spinal cord that carry sensory impulses to the brain.

**association area** (ah-so″se-a′shun a′re-ah) Region of the cerebral cortex controlling memory, reasoning, judgment, and emotions.

**astrocyte** (as′tro-sīt) Type of neuroglia that connects neurons to blood vessels in the CNS.

**atmospheric pressure** (at″mos-fēr′ik presh′ur) Pressure exerted by the weight of air, about 760 millimeters of mercury at sea level.

**atom** (at′om) Smallest particle of an element that has the properties of that element.

**atomic number** (ah-tom′ik num′ber) Number of protons in an atom of an element.

**atomic weight** (ah-tom′ik wāt) The number of protons and neutrons in an atom of an element.

**ATP** Adenosine triphosphate.

**ATPase** Enzyme that releases energy stored in the terminal phosphate bonds of ATP molecules.

**atrium** (a′tre-um) (plural, *atria*) Upper chamber of the heart.

**atrioventricular bundle** (a″tre-o-ven-trik′u-lar bun′dl) **(AV bundle)** Group of specialized muscle fibers that conducts impulses from the atrioventricular node to the ventricular muscle of the heart.

**atrioventricular node** (a″tre-o-ven-trik′u-lar nōd) **(AV node)** Specialized mass of cardiac muscle fibers in the interatrial septum of the heart that transmits cardiac impulses from the sinoatrial node to the AV bundle.

**auditory ossicle** (aw′di-to″re os′i-kl) Bone of the middle ear.

**auditory tube** (aw′di-to″re tūb) Tube that connects the middle ear cavity to the pharynx; Eustachian tube.

**auricle** (aw′ri-kl) An earlike structure; the part of the heart that forms the wall of an atrium.

**autonomic nervous system** (aw″to-nom′ik ner′vus sis′tem) Part of nervous system that controls the viscera.

**autosome** (aw′to-sōm) One of the 22 chromosomes that does not include a gene that determines sex.

**axial** (ak′se-al) Pertaining to the head, neck, and trunk.

**axillary** (ak′sĭ-ler″e) Pertaining to the armpit.

**axon** (ak′son) A nerve fiber. It conducts an impulse away from the neuron cell body.

## B

**B cell** (sel) Lymphocyte that produces and secretes antibodies that bind and destroy foreign antigens; B lymphocyte.

**baroreceptor** (bar″o-re-sep′tor) Sensory receptor in a blood vessel wall stimulated by changes in blood pressure.

**basal ganglia** (ba′sal gang′lē-ah) Mass of gray matter deep within a cerebral hemisphere of the brain.

**base** (bās) Substance that ionizes in water, releasing hydroxide ions ($OH^-$) or other ions that combine with hydrogen ions.

**basement membrane** (bās′ment mem′brān) Layer of nonliving material that anchors epithelial tissue to underlying connective tissue.

**basophil** (ba′so-fil) White blood cell containing cytoplasmic granules that stain with basic dye.

**beta oxidation** (ba′tah ok″sĭ-da′shun) Chemical process that breaks fatty acids down to form molecules of acetyl coenzyme A, which enters the citric acid cycle.

**bile** (bīl) Fluid secreted by the liver and stored in the gallbladder.

**bile duct** (bīl dukt) Tube that transports bile from the cystic duct and common hepatic duct to the duodenum.

**bilirubin** (bil″ĭ-roo′bin) A bile pigment produced from hemoglobin breakdown.

**biliverdin** (bil″ĭ-ver′din) A bile pigment produced from hemoglobin breakdown.

**blastocyst** (blas′to-sist) Early stage of prenatal development when the embryo is a hollow ball of cells.

**blood** (blud) A connective tissue consisting of cells in a liquid matrix called plasma that circulate through the heart and vessels carrying substances throughout the body.

**bone** (bōn) A hard, mineralized connective tissue that forms the bones of the skeleton.

**brachial** (bra′ke-al) Pertaining to the arm.

**brainstem** (brānstem) Part of the brain that includes the midbrain, pons, and medulla oblongata.

**bronchial tree** (brong′ke-al tre) The bronchi and their branches that carry air between the trachea and the alveoli of the lungs.

**bronchiole** (brong′ke-ōl) Small branches of bronchi in the lung.

**bronchus** (brong′kus) (plural, *bronchi*) Branch of the trachea that leads to a lung.

**buccal** (buk′al) Pertaining to the mouth and inner lining of the cheeks.

**buffer** (buf′er) Substance that can react with a strong acid or base to form a weaker acid or base and thus resist a change in pH.

**bulbourethral gland** (bul″bo-u-re′thral gland) Gland that secretes viscous fluid into the male urethra during sexual excitement; Cowper's gland.

**bursa** (ber′sah) (plural, *bursae*) Saclike, fluid-filled structure, lined with synovial membrane, near a joint.

## C

**calcitonin** (kal″sĭ-to′nin) Hormone from the thyroid gland that helps regulate blood calcium concentration.

**calorie** (kal′o-re) Unit that measures heat energy and the energy content of foods.

**canaliculus** (kan″ah-lik′u-lus) Microscopic canal that connects lacunae of bone tissue.

**capacitation** (kah-pas″i-ta′shun) Activation of a sperm cell to fertilize an egg cell.

**capillary** (kap′ĭ-lar″e) Small blood vessel that connects an arteriole and a venule.

**carbaminohemoglobin** (kar-bam″ĭ-no-he″mo-glo′bin) Bonded carbon dioxide and hemoglobin.

**carbohydrate** (kar″bo-hi′drāt) Organic compound consisting of carbon, hydrogen, and oxygen, in a 1:2:1 ratio.

**carbonic anhydrase** (kar-bon′ik an-hi′drās) Enzyme that catalyzes the reaction between carbon dioxide and water to form carbonic acid.

**carboxypeptidase** (kar-bok″se-pep′tĭ-dās) Protein-splitting enzyme in pancreatic juice.

**cardiac conduction system** (kar′de-ak kon-duk′shun sis′tem) System of specialized cardiac muscle fibers that conducts cardiac impulses from the SA node into the myocardium.

**cardiac cycle** (kar′de-ak si′kl) Sequence of myocardial contraction and relaxation that constitutes a complete heartbeat.

**cardiac muscle tissue** (kar′de-ak mus′l tish′u) Specialized muscle tissue found only in the heart.

**cardiac output** (kar′de-ak owt′poot) The volume of blood per minute that the heart pumps (stroke volume in milliliters multiplied by heart rate in beats per minute).

**cardiovascular** (kahr″de-o-vas′ku-lur) Pertaining to the heart and blood vessels.

**carpal** (kar′pal) Wrist bone.

**cartilage** (kar′ti-lij) Type of connective tissue in which cells are in lacunae separated by a semisolid extracellular matrix.

**cartilaginous joint** (kar-tĭ-laj′ĭ-nus joint) Two or more bones joined by cartilage.

**catabolism** (kă-tab′o-lizm) Breakdown of large molecules; catabolic metabolism.

**catalyst** (kat′ah-list) Chemical that increases the rate of a chemical reaction, but is not permanently altered by the reaction.

**celiac** (se′le-ak) Pertaining to the abdomen.

**cell** (sel) The structural and functional unit of an organism.

**cell body** (sel bod′e) Part of a nerve cell that includes a cytoplasmic mass and a nucleus, and from which nerve processes extend.

**cell membrane** (sel mem′brān) The selectively permeable outer boundary of a cell consisting of a phospholipid bilayer embedded with proteins.

**cellular immune response** (sel′u-lar i-mūn′ ri-spons′) The body's attack of T cells and their secreted products on nonself antigens.

**cellular respiration** (sel′u-lar res″pĭ-ra′shun) A biochemical pathway that releases energy from organic compounds.

**cellulose** (sel′u-lōs) Polysaccharide abundant in plant tissues that human digestive enzymes cannot break down.

**cementum** (se-men′tum) Bonelike material that fastens the root of a tooth into its bony socket.

**central canal** (sen′tral kah-nal′) Tiny channel in bone tissue that houses a blood vessel; tube in the spinal cord continuous with brain ventricles and contains cerebrospinal fluid.

**central nervous system** (sen′tral ner′vus sis′tem) **(CNS)** The brain and spinal cord.

**centriole** (sen′tre-ōl) Cellular structure built of microtubules that organizes the mitotic spindle.

**centromere** (sen′tro-mēr) Region of chromosome where spindle fibers attach during mitosis.

**centrosome** (sen′tro-sōm) Cellular organelle consisting of two centrioles.

**cephalic** (sĕ-fal′ik) Pertaining to the head.

**cerebellar cortex** (ser″ĕ-bel′ar kor′teks) Outer layer of the cerebellum.

**cerebellum** (ser″ĕ-bel′um) Part of the brain that coordinates skeletal muscle movement.

**cerebral cortex** (ser′ĕ-bral kor′teks) Outer layer of the cerebrum.

**cerebral hemisphere** (ser′ĕ-bral hem′ĭ-sfēr) One of the large, paired structures that constitute the cerebrum.

**cerebrospinal fluid** (ser″ĕ-bro-spi′nal floo′id) **(CSF)** Fluid in the ventricles of the brain, subarachnoid space of the meninges, and the central canal of the spinal cord.

**cerebrum** (ser′ĕ-brum) Part of the brain in the upper part of the cranial cavity that provides higher mental functions.

**cervical** (ser′vĭ-kal) Pertaining to the neck.

**cervix** (ser′viks) Narrow, inferior end of the uterus that leads into the vagina.

**chemical bond** (kem′ĭkel bond) Attractive force holding atoms together.

**chemistry** (kem′is-trē) The study of matter.

**chemoreceptor** (ke″mo-re-sep′tor) Receptor stimulated by the binding of certain chemicals.

**chief cell** (chēf sel) Cell type in a gastric gland that secretes digestive enzymes.

**cholecystokinin** (ko″le-sis″to-ki′nin) Hormone the small intestine secretes that stimulates release of pancreatic juice from the pancreas and bile from the gallbladder.

**cholesterol** (ko-les′ter-ol) A lipid that some cells produce and use to synthesize steroid hormones.

**cholinergic fiber** (ko″lin-er′jik fi′ber) Axon that secretes acetylcholine at its terminal.

**chondrocyte** (kon′dro-sīt) A cartilage cell.

**chordae tendineae** (kor′de ten′dĭ-ne) Fibrous strings attached to the cusps of the tricuspid and mitral valves in the heart.

**chorion** (ko′re-on) Extraembryonic membrane that forms the outermost covering around a fetus and contributes to formation of the placenta.

**chorionic villus** (ko″re-on′ik vil′us) Projection that extends from the outer surface of the chorion and helps attach an embryo to the uterine wall.

**choroid coat** (ko′roid kōt) Vascular, pigmented middle layer of the wall of the eye.

**choroid plexus** (ko′roid plek′sus) Mass of specialized capillaries that secretes cerebrospinal fluid into a brain ventricle.

**chromatid** (kro′mah-tid) One longitudinal half of a replicated chromosome.

**chromatin** (kro′mah-tin) DNA and complexed protein that condenses to form chromosomes during mitosis.

**chromatophilic substance** (kro″mah-to-fil′ik sub′stans) **(Nissl bodies)** Membranous sacs in the cytoplasm of nerve cells that have ribosomes attached to their surfaces.

**chromosome** (kro′mo-sōm) Rodlike structure that condenses from chromatin in a cell's nucleus during mitosis.

**chylomicron** (ki″lo-mi′kron) Microscopic droplet of fat in the blood that forms following fat digestion.

**chyme** (kīm) Semifluid mass of partially digested food that passes from the stomach to the small intestine.

**chymotrypsin** (ki″mo-trip′sin) A protein-splitting enzyme in pancreatic juice.

**cilia** (sil′e-ah) Microscopic, hairlike processes on the exposed surfaces of certain epithelial cells.

**ciliary body** (sil′e-er″e bod′e) Structure associated with the choroid layer of the eye that secretes aqueous humor and houses the ciliary muscle.

**circadian rhythm** (ser″kah-de′an rithm) Pattern of repeated behavior associated with cycles of night and day.

**cisterna** (sis-ter′nah) Enlarged portion of the sarcoplasmic reticulum near the actin and myosin filaments of a muscle fiber.

**citric acid cycle** (sit′rik as′id si′kl) Series of chemical reactions that oxidizes certain molecules, releasing energy; Krebs cycle.

**cleavage** (klēv′ij) Early successive divisions of the zygote into a ball of progressively smaller cells.

**clitoris** (klit′o-ris) Small, erectile organ in the anterior vulva; corresponding to the penis.

**clone** (klōn) Group of cells that descend from a single cell and are therefore genetically identical to it.

**CNS** Central nervous system.

**coagulation** (ko-ag″u-la′shun) Blood clotting.

**cochlea** (kok′le-ah) Portion of inner ear that has hearing receptors.

**codon** (ko′don) Set of three contiguous nucleotides of a messenger RNA molecule that specifies a particular amino acid.

**coenzyme** (ko-en′zīm) Nonprotein organic molecule required for the activity of a particular enzyme.

**cofactor** (ko′fak-tor) Small molecule or ion that must combine with an enzyme for activity.

**collagen fiber** (kol′ah-jen-us fi′ber) White fiber consisting of the protein collagen, common in connective tissues, including bone matrix.

**common hepatic duct** (kom′mon hepat′ik dukt) Tube that transports bile from the liver to the bile duct.

**compact bone** (kom′-pakt bōn) Dense tissue in which cells are organized in osteons without apparent spaces.

**complement** (kom′ple-ment) Group of proteins activated when an antibody binds an antigen; enhances reaction against nonself substances.

**complete protein** (kom-plēt′ pro′te-in) Protein that contains adequate amounts of the essential amino acids to maintain body tissues and to promote normal growth and development.

**compound** (kom′pownd) Substance composed of two or more chemically bonded elements.

**cone** (kōn) Color receptor in the retina of the eye.

**conformation** (kon″for-ma″shen) Three-dimensional form of a protein.

**conjunctiva** (kon″junk-ti′vah) Membranous covering on the anterior surface of the eye and lining the eyelids.

**connective tissue** (kŏ-nek′tiv tish′u) Basic type of tissue that consists of cells within an extracellular matrix. Connective tissues include bone, cartilage, and blood.

**convergence** (kon-ver′jens) Two or more neurons forming synapses with the same neuron.

**cornea** (kor′ne-ah) Transparent anterior portion of the outer layer of the eye wall.

**coronary artery** (kor′o-na″re ar′ter-e) An artery that supplies blood to the wall of the heart.

**coronary sinus** (kor′o-na″re si′nus) Large vessel on the posterior surface of the heart into which cardiac veins drain.

**corpus callosum** (kor′pus kah-lo′sum) Mass of white matter in the brain composed of nerve fibers connecting the right and left cerebral hemispheres.

**corpus luteum** (kor′pus loot′e-um) Structure that forms from the tissues of a ruptured ovarian follicle and secretes female hormones.

**cortisol** (kor′tĭ-sol) Glucocorticoid secreted by the adrenal cortex.

**costal** (kos′tal) Pertaining to the ribs.

**covalent bond** (ko′va-lent bond) Chemical bond formed by electron sharing between atoms.

**cranial nerve** (kra′ne-al nerv) Nerve that arises from the brain or brainstem.

**creatine phosphate** (kre′ah-tin fos′fāt) Muscle biochemical that stores energy.

**crista ampullaris** (kris′tah am-pul′ar-is) Sensory organ in a semicircular canal that functions in the sense of dynamic equilibrium.

**cubital** (ku′bi-tal) Pertaining to the elbow.

**cutaneous** (ku-ta′ne-us) Pertaining to the skin.

**cyclic AMP** (si′klik a-em-pē) **(cAMP)** A second messenger molecule in a signal transduction pathway.

**cystic duct** (sis′tik dukt) Tube that connects the gallbladder to the bile duct.

**cytocrine secretion** (si′to-krin se-kre′shun) Transfer of melanin granules from melanocytes into epithelial cells.

**cytokinesis** (si″to-kĭ-ne′sis) Division of the cytoplasm during cell division.

**cytoplasm** (si′to-plazm) The contents of a cell including the gel-like cytosol and organelles, excluding the nucleus, enclosed by the cell membrane.

**cytoskeleton** (si″to-skel′e-ten) A cell's framework of protein filaments and tubules.

## D

**deamination** (de-am″ĭ-na′shun) Removing amino groups (–$NH_2$) from amino acids.

**decomposition** (de″-kom-po-zish′un) Breakdown of molecules.

**dehydration synthesis** (de″hi-dra′shun sin′thĕ-sis) Anabolic process that joins small molecules by releasing the equivalent of a water molecule; synthesis.

**dendrite** (den′drīt) Process of a neuron that receives input from other neurons.

**dense connective tissue** (dens kō-nek′tiv tish′u) A connective tissue with many collagenous fibers, a fine network of elastin fibers, and sparse fibroblasts.

**dentin** (den′tin) Bonelike substance that forms the bulk of a tooth.

**deoxyhemoglobin** (de-ok″se-he″mo-glo′bin) Hemoglobin that has not bound oxygen.

**deoxyribonucleic acid** (de-ok′si-ri″bo-nu-kle″ik as′id) **(DNA)** The genetic material; a double-stranded polymer of nucleotides, each containing a phosphate group, a nitrogenous base (adenine, thymine, guanine, or cytosine), and the sugar deoxyribose.

**depolarization** (de-po″lar-ĭ-za′shun) A change in membrane potential from negative to more positive.

**dermis** (der′mis) The thick layer of the skin beneath the epidermis.

**descending tract** (de-send′ing trakt) Group of nerve fibers that carries impulses from the brain down through the spinal cord.

**detrusor muscle** (de-trūz′or mus′l) Muscular wall of the urinary bladder.

**diapedesis** (di″ah-pĕ-de′sis) Squeezing of leukocytes between the cells of blood vessel walls.

**diaphragm** (di′ah-fram) A sheetlike structure largely composed of skeletal muscle and connective tissue that separates the thoracic and abdominal cavities; a contraceptive device inserted in the vagina.

**diaphysis** (di-af′ĭ-sis) Shaft of a long bone.

**diastole** (di-as′to-le) Phase of the cardiac cycle when a heart chamber wall relaxes.

**diastolic pressure** (di-a-stol′ik presh′ur) Lowest arterial blood pressure reached during the diastolic phase of the cardiac cycle.

**diencephalon** (di″en-sef′ah-lon) Part of the brain in the region of the third ventricle that includes the thalamus and hypothalamus.

**differentiation** (dif″er-en″she-a′shun) Cell specialization.

**diffusion** (dĭ-fu′zhun) Random movement of molecules from a region of higher concentration toward one of lower concentration.

**digestion** (di-jest′yun) Breaking down of large nutrient molecules into molecules small enough to be absorbed; hydrolysis.

**dipeptide** (di-pep′tīd) Molecule composed of two joined amino acids.

**disaccharide** (di-sak′ah-rīd) Sugar produced by the union of two monosaccharides.

**distal** (dis′tal) Further from a point of attachment; opposite of *proximal.*

**divergence** (di-ver′jens) Spreading apart. A single neuron forming synapses with two or more postsynaptic cells.

**DNA** Deoxyribonucleic acid; the genetic material.

**dominant** (dom′eh-nant) A type of allele that is expressed over a recessive allele.

**dorsal** (dors′al) Pertaining to the back surface of a body part.

**dorsal root** (dor′sal root) Sensory branch of a spinal nerve by which it joins the spinal cord.

**ductus arteriosus** (duk′tus ar-te″re-o′sus) Blood vessel that connects the pulmonary artery and the aorta in a fetus.

**ductus deferens** (duk′tus def″er-ens) (plural, *ductus deferentia*) Tube that leads from the epididymis to the urethra of the male reproductive tract.

**ductus venosus** (duk′tus ven-o′sus) Blood vessel that connects the umbilical vein and the inferior vena cava in a fetus.

**dura mater** (du′rah ma′ter) Tough outer layer of the meninges.

**dynamic equilibrium** (di-nam′ik e″kwĭ-lib′re-um) Maintenance of balance when the head and body are suddenly moved or rotated.

## E

**eardrum** (er′drum) Tympanic membrane; a thin membrane that separates the external ear from the middle ear.

**eccrine gland** (ek′rin gland) Sweat gland that maintains body temperature.

**ECG** Electrocardiogram.

**ectoderm** (ek′to-derm) Outermost primary germ layer of the embryo.

**edema** (ĕ-de′mah) Fluid accumulation in tissue spaces.

**effector** (e-fek′tor) A muscle or gland that effects change in the body.

**efferent arteriole** (ef′er-ent ar-te′re-ōl) The vessel that conducts blood away from the glomerulus of each nephron.

**ejaculation** (e-jak″u-la′shun) Discharge of sperm-containing semen from the male urethra.

**elastic cartilage** (ē-las-tik kar′-ti-lij) Opaque, flexible connective tissue with many elastic fibers.

**elastic fibers** (e-las′tic fiberz) Stretchy yellow connective tissue fibers consisting of the protein elastin.

**electrocardiogram** (e-lek″tro-kar′de-o-gram″) **(ECG)** Recording of the electrical activity associated with the cardiac cycle.

**electrolyte** (e-lek′tro-līt) Substance that ionizes in a water solution.

**electrolyte balance** (e-lek′tro-līt bal′ans) Condition when electrolytes entering the body equal those leaving it.

**electron** (e-lek′tron) Small, negatively charged particle that encircles the nucleus of an atom.

**electron transport chain** (e-lektron tranz′port chān) Series of metabolic reactions that takes high-energy electrons from glycolysis and the citric acid cycle to form ATP, water, $CO_2$, and heat.

**element** (el′ĕ-ment) Chemical substance with only one type of atom.

**embolus** (em′bo-lus) Blood clot or gas bubble carried in circulation that may obstruct a blood vessel.

**embryo** (em′bre-o) Offspring development from about the time of implantation through the eighth week of prenatal development.

**emission** (e-mish′un) Movement of sperm cells from the ductus deferentia into the ejaculatory ducts and urethra.

**emulsification** (e-mul″sĭ-fĭ-ka′shun) Breaking up of fat globules into smaller droplets by the action of bile salts.

**enamel** (e-nam′el) Hard covering on the exposed surface of a tooth.

**endocardium** (en″do-kar′de-um) Inner lining of the heart chambers.

**endochondral bone** (en″do-kon′dral bōn) Bone that begins as hyaline cartilage that is subsequently replaced by bone tissue.

**endocrine gland** (en′do-krin gland) Gland that secretes hormones directly into the blood.

**endocytosis** (en″do-si-to′sis) Process by which a cell membrane envelops a substance and draws it into the cell in a vesicle.

**endoderm** (en′do-derm) The innermost primary germ layer in the embryo.

**endolymph** (en′do-limf) Fluid in the membranous labyrinth of the inner ear.

**endometrium** (en″do-me′tre-um) Inner lining of the uterus.

**endomysium** (en″do-mis′e-um) Sheath of connective tissue surrounding each skeletal muscle fiber.

**endoplasmic reticulum** (en′do-plaz mik rĕ-tik′u-lum) Organelle composed of a network of connected membranous tubules and vesicles.

**endosteum** (en-dos′te-um) Tissue lining the medullary cavity in a bone.

**endothelium** (en″do-the′le-um) Layer of epithelial cells that forms the inner lining of blood vessels and heart chambers.

**energy** (en′er-je) An ability to move something and thus do work.

**enzyme** (en′zīm) Protein that catalyzes a specific biochemical reaction.

**eosinophil** (e″o-sin′o-fil) White blood cell containing cytoplasmic granules that stain with acidic dye.

**ependyma** (ĕ-pen′dĭ-mah) Neuroglia that line the ventricles of the brain.

**epicardium** (ep″ĭ-kar′de-um) Visceral part of the pericardium on the surface of the heart.

**epidermis** (ep″i-der′mis) Outer epithelial layer of the skin.

**epididymis** (ep″ĭ-did′ĭ-mis) (plural, *epididymides*) Highly coiled tube that leads from the seminiferous tubules of the testis to the ductus deferens.

**epidural space** (ep″ĭ-du′ral spās) Space between the dural sheath of the spinal cord and the bone of the vertebral canal.

**epigastric region** (ep″ĭ-gas′trik re′jun) Upper middle part of the abdomen.

**epiglottis** (ep″ĭ-glot′is) Flaplike, cartilaginous structure at the back of the tongue near the entrance to the trachea.

**epimysium** (ep″i-mis′e-um) Outer sheath of connective tissue surrounding a skeletal muscle.

**epinephrine** (ep″ĭ-nef′rin) Hormone the adrenal medulla secretes during times of stress.

**epiphyseal plate** (ep″ĭ-fiz′e-al plāt) Cartilaginous layer between the epiphysis and diaphysis of a long bone that grows, lengthening the bone.

**epiphysis** (ĕ-pif′ĭ-sis) End of a long bone.

**epithelial tissue** (ep″ĭ-the′le-al tish′u) Tissue that covers all external and lines all internal body surfaces. Varieties are classified by cell shape (squamous, cuboidal, or columnar) and number of layers (simple, stratified, or pseudostratified).

**erythrocyte** (ĕ-rith′ro-sīt) Red blood cell.

**erythropoietin** (ĕ-rith″ro-poi′ĕ-tin) Kidney hormone that promotes red blood cell formation.

**esophagus** (ĕ-sof′ah-gus) Tubular part of the digestive tract connecting the pharynx to the stomach.

**essential amino acid** (ĕ-sen′shal ah-me′no as′id) Amino acid required for health that body cells cannot synthesize in adequate amounts.

**essential fatty acid** (ĕ-sen′shal fat′e as′id) Fatty acid required for health that body cells cannot synthesize in adequate amounts.

**estrogens** (es′tro-jenz) Group of hormones that stimulates the development of female secondary sex characteristics.

**eumelanin** (u-mel′ah-nin) Brownish-black pigment.

**eversion** (e-ver′zhun) Turning the sole of the foot outward away from the midline.

**exchange reaction** (eks-chānj re-ak′shun) Chemical reaction in which parts of two kinds of molecules trade positions.

**exocrine gland** (ek′so-krin gland) Gland that secretes its products into ducts or onto an outside body surface.

**exocytosis** (ek″so-si-tōsis) Transport of substances out of a cell in membrane-bounded vesicles.

**expiration** (ek″spĭ-ra′shun) Breathing out; exhalation.

**extension** (ek-sten′shun) Movement increasing the angle between parts at a joint.

**extracellular fluid** (eks″trah-sel′u-lar floo′id) Body fluid outside cells.

**extracellular matrix** (eks″trah-sel′u-lar ma′triks) Molecules that fill spaces between cells, consisting mostly of protein fiber networks.

**extrapyramidal tract** (ek″strah-pĭ-ram′i-dal trakt) Nerve tracts, other than the corticospinal tracts, that transmit impulses from the cerebral cortex to the spinal cord.

## F

**facilitated diffusion** (fah-sil″ĭ-tāt′ed dĭ-fu′zhun) Diffusion in which a carrier molecule transports a substance across a cell membrane from a region of higher concentration to a region of lower concentration.

**facilitation** (fah-sil″ĭ-ta′shun) Subthreshold stimulation of a neuron that increases responsiveness to further stimulation.

**fascia** (fash′e-ah) Sheet of dense connective tissue that encloses a muscle.

**fat** (fat) Adipose tissue; an organic molecule that includes glycerol and fatty acids.

**fatty acid** (fat′e as′id) Building block of a fat molecule.

**feces** (fe′sēz) Material expelled from the digestive tract during defecation.

**fertilization** (fer″tĭ-lĭ-za′shun) Union of an egg cell and a sperm cell.

**fetus** (fe′tus) Prenatal human after eight weeks of development.

**fibrin** (fi′brin) Insoluble, fibrous protein formed from fibrinogen during blood coagulation.

**fibrinogen** (fi-brin′o-jen) Plasma protein converted into fibrin during blood coagulation.

**fibroblast** (fi′bro-blast) Cell that produces fibers in connective tissues.

**fibrocartilage** (fi′bro kar′tĭ-lij) Strongest and most durable cartilage; made up of cartilage cells and many collagenous fibers.

**fibrous joint** (fi′brus joint) Two or more bones joined by dense connective tissue.

**filtration** (fil-tra′shun) Movement of material through a membrane as a result of hydrostatic pressure.

**fissure** (fish′ur) Narrow cleft separating parts, such as the lobes of the cerebrum.

**flagellum** (fla-jel′um) Relatively long, motile process that extends from the surface of a sperm cell.

**flexion** (flek′shun) Bending at a joint that decreases the angle between bones.

**follicle-stimulating hormone** (fol′ĭ-kl stim′u-la″ting hor′mōn) **(FSH)** Hormone secreted by the anterior pituitary to stimulate development of an ovarian follicle in a female or sperm cell production in a male.

**follicular cell** (fŏ-lik′u-lar sel) Ovarian cell that surrounds a developing oocyte and secretes female sex hormones.

**fontanel** (fon″tah-nel′) Membranous region between certain developing cranial bones in the skull of a fetus or infant.

**foramen magnum** (fo-ra′men mag′num) Opening in the occipital bone of the skull through which the spinal cord passes.

**foramen ovale** (fo-ra′men o-val′e) Opening in the interatrial septum of the fetal heart.

**fovea centralis** (fo′ve-ah sen-tral′is) Depressed region of the retina, consisting of densely packed cones, that provides the greatest visual acuity.

**free nerve endings** (frē nerv end-ingz) Receptors abundant in epithelium, associated with sensing temperature and pain.

**frontal** (frun′tal) Plane that divides a structure into anterior and posterior portions, pertaining to the forehead.

**FSH** Follicle-stimulating hormone.

**functional syncytium** (funk′shun-al sin-sish′e-um) Merging cells that function as a unit; those of the heart are joined electrically.

## G

**gallbladder** (gawl′blad-er) Saclike organ associated with the liver that stores and concentrates bile.

**ganglion** (gang′glē-on) (plural, *ganglia*) Mass of neuron cell bodies, usually outside the central nervous system.

**gastric gland** (gas′trik gland) Gland in the stomach wall that secretes gastric juice.

**gastric juice** (gas′trik jo͞os) Secretion of the gastric glands in the stomach.

**gastrin** (gas′trin) Hormone secreted by the stomach lining that stimulates gastric juice secretion.

**gene** (jēn) Part of a DNA molecule that encodes information to synthesize a protein, a control sequence, or tRNA or rRNA; the unit of inheritance.

**genetic code** (jĕ-net′ik kōd) Information for synthesizing proteins encoded in the nucleotide sequence of DNA molecules.

**genome** (je′nōm) Complete set of genetic instructions for an organism.

**genotype** (jē-no-tīp) The alleles (gene variants) of a particular gene in an individual.

**GH** Growth hormone.

**globulin** (glob′u-lin) Type of protein in blood plasma.

**glomerular capsule** (glo-mer′u-lar kap′sūl) Double-walled enclosure of the glomerulus of a nephron; Bowman's capsule.

**glomerulus** (glo-mer′u-lus) Filtering capillary tuft in the glomerular capsule of a nephron.

**glottis** (glot′is) Slitlike opening between the true vocal folds or vocal cords.

**glucagon** (gloo′kah-gon) Hormone secreted by the pancreatic islets that releases glucose from glycogen.

**glucocorticoid** (gloo″ko-kor′tĭ-koid) Any of several hormones that the adrenal cortex secretes that affects carbohydrate, fat, and protein metabolism.

**glucose** (gloo′kōs) Monosaccharide in blood that is the primary source of cellular energy.

**gluteal** (gloo′te-al) Pertaining to the buttocks.

**glycerol** (glis′er-ol) Organic compound that is a building block for fat molecules.

**glycogen** (gli′ko-jen) Polysaccharide that stores glucose in the liver and muscles.

**glycolysis** (gli-kol′ĭ-sis) The energy-releasing breakdown of glucose to produce 2 pyruvic acid molecules and a net of 2 ATP.

**goblet cell** (gob′let sel) Epithelial cell specialized to secrete mucus in the respiratory tract and intestines.

**Golgi apparatus** (gol′je ap″ah-ra′tus) Organelle that prepares and modifies cellular products for secretion.

**gonadotropin** (go-nad″o-trōp′in) Hormone that stimulates activity in the gonads (testes and ovaries).

**granulocyte** (gran′u-lo-sīt) Leukocyte with granules in the cytoplasm.

**growth hormone** (grōth hor′mōn) **(GH)** Hormone released by the anterior pituitary that promotes growth of the organism; somatotropin.

**gyrus** (ji′rus) (pl. *gyri*) Elevation on the brain's surface; convolution.

## H

**hair follicle** (hār fol′ĭ-kl) Tubelike depression in the epidermis in which a hair develops.

**haploid** (hap′loyd) Sex cell with half of the normal number of chromosomes, in humans 23.

**hapten** (hap′ten) Small molecule that combines with a larger one, forming an antigen.

**hematocrit** (he-mat′o-krit) **(HCT)** The percentage by volume of red blood cells in a sample of whole blood.

**hematopoiesis** (he″-mă-to-poi-e′sis) Production of blood cells from dividing stem and progenitor cells.

**heme** (hēm) Iron-containing part of a hemoglobin molecule.

**hemoglobin** (he″mo-glo′bin) Oxygen-carrying pigment in red blood cells.

**hemostasis** (he″mo-sta′sis) Stoppage of bleeding.

**hepatic lobule** (hĕ-pat′ik lob′ul) Functional unit of the liver.

**heterozygous** (het′er-o-zi′gus) Different alleles in a gene pair.

**holocrine gland** (ho′lo-krin gland) Gland whose secretion contains entire secretory cells.

**homeostasis** (ho″me-o-sta′sis) Dynamic state in which the body's internal environment is maintained in the normal range.

**homozygous** (ho′mo-zi′gus) Identical alleles in a gene pair.

**hormone** (hor′mōn) Substance secreted by an endocrine gland and transported in the blood which has actions on target cells.

**humoral immune response** (hu′mor-al i-mūn′ ri-spons′) Circulating antibodies' destruction of cells bearing nonself antigens.

**hyaline cartilage** (hī-ah-lin kar′ti-lij) Semitransparent, flexible connective tissue with an ultra-fine fiber matrix.

**hydrogen bond** (hi′dro-jen bond) Weak bond between a hydrogen atom and an atom of oxygen or nitrogen between molecules or different regions of a very large molecule.

**hydrolysis** (hi-drol′ĭ-sis) Enzymatically adding a water molecule to split a molecule.

**hydrostatic pressure** (hy″dro-stat′ik presh′ur) Pressure exerted by fluids, such as blood pressure.

**hymen** (hi′men) Membranous fold of tissue that partially covers the vaginal opening.

**hypertonic** (hi″per-ton′ik) Solution with a greater osmotic pressure than the solution (usually body fluids) to which it is compared.

**hyperventilation** (hi″per-ven″tĭ-la′shun) Deep and rapid breathing that lowers blood $CO_2$ levels.

**hypochondriac regions** (hi″po-kon′dre-ak re′jun) Portion of the abdomen on either side of the upper middle or epigastric region.

**hypogastric region** (hi″po-gas′trik re′jun) Lower middle portion of the abdomen.

**hypothalamus** (hi″po-thal′ah-mus) Part of the brain below the thalamus and forming the floor of the third ventricle.

**hypotonic** (hi″po-ton′ik) Solution with a lower osmotic pressure than the solution (usually body fluids) to which it is compared.

## I

**iliac region** (il′e-ak re′jun) Portion of the abdomen on either side of the lower middle or hypogastric region.

**ilium** (il′e-um) One of the bones making up the hip bone.

**immunity** (ĭ-mu′nĭ-te) Resistance to the effects of specific disease-causing agents.

**immunoglobulin** (im″u-no-glob′u-lin) Globular plasma protein that functions as an antibody.

**impulse** (im′puls) An action potential.

**incomplete protein** (in″kom-plēt′ pro′te-in) Protein with inadequate amounts of essential amino acids.

**inferior** (in-fer′e-or) Situated below something else; pertaining to the lower surface of a part.

**inflammation** (in″flah-ma′shun) Tissue response to stress that dilates blood vessels and accumulates fluid in the affected region.

**inguinal** (ing′gwĭ-nal) Pertaining to the groin region.

**innate defense** (in′ate dē-fens) Inborn, nonspecific defense that blocks entry of or destroys pathogens.

**inorganic** (in″or-gan′ik) Chemical substances that do not include carbon and hydrogen atoms.

**insertion** (in-ser′shun) End of a muscle attached to a movable part.

**inspiration** (in″spĭ-ra′shun) Breathing in; inhalation.

**insula** (in′su-lah) Cerebral lobe deep within the lateral sulcus.

**insulin** (in′su-lin) Hormone the pancreatic islets secrete that stimulates cells to take up glucose.

**integumentary system** (in-teg-u-men′tar-e sis′tem) The skin and its accessory structures.

**intercalated disc** (in-ter″kah-lāt′ed disk) Membranous boundary between cardiac muscle cells.

**internal environment** (in-ter′nĕl en-vi-ruhment) Conditions and elements that make up the inside of the body, surrounding the cells.

**interneuron** (in″ter-nu′ron) Neuron between a sensory neuron and a motor neuron; internuncial or association neuron.

**interphase** (in′ter-fāz) Period between cell divisions when a cell metabolizes and prepares to divide.

**interstitial cell** (in″ter-stish′al sel) Hormone-secreting cell between seminiferous tubules of the testis.

**intervertebral disc** (in″ter-ver′tĕ-bral disk) Layer of fibrocartilage between bodies of adjacent vertebrae.

**intestinal gland** (in-tes′tĭ-nal gland) Tubular gland at the base of a villus in the intestinal wall.

**intestinal villus** (in-tes′tĭ-nal vil′us) (plural, *intestinal villi*) Fingerlike extension of the small intestinal lining.

**intracellular fluid** (in″trah-sel′u-lar floo′id) The liquid portion of the cell; cytosol.

**intramembranous bone** (in″trah-mem′brah-nus bōn) Bone that forms from membranelike layers of primitive connective tissue.

**intrinsic factor** (in-trin′sik fak′tor) Substance produced by the gastric glands necessary for absorption of vitamin B12.

**inversion** (in-ver′zhun) Turning the sole of the foot inward toward the midline.

**ion** (i′on) Electrically charged atom or molecule.

**ionic bond** (i-on′ik bond) Chemical bond that results when two ions form by transfer of electrons.

**iris** (i′ris) Colored, muscular part of the eye around the pupil that regulates its size.

**isotonic** (i″so-ton′ik) Solution with the same osmotic pressure as the solution (usually body fluids) to which it is compared.

**isotope** (i′so-tōp) Atom that has the same number of protons as other atoms of the same element but a different number of neutrons in its nucleus.

## J

**joint** (joy′-nt) Union of two or more bones; articulation.

**juxtaglomerular apparatus** (juks″tah-glo-mer′u-lar ap″ah-ra′tus) A group of cells in the wall of the afferent arteriole in the kidney that plays a role in the control of renin secretion.

## K

**keratin** (ker′ah-tin) Intracellular protein in epidermis, hair, and nails.

**keratinization** (ker″ah-tin′i-za′shun) Process by which cells form fibrils of keratin and harden.

**ketone body** (ke′tōn bod′e) Compound produced during fat catabolism.

**Kupffer cell** (koop′fer sel) Large, fixed phagocyte in the liver that removes bacterial cells from the blood.

## L

**labyrinth** (lab′ĭ-rinth) System of connecting tubes in the inner ear, including the cochlea, vestibule, and semicircular canals.

**lacrimal gland** (lak′rĭ-mal gland) Tear-secreting gland.

**lactase** (lak′tās) Enzyme that catalyzes the breakdown of lactose into glucose and galactose.

**lacteal** (lak′te-al) Lymphatic capillary associated with a villus of the small intestine.

**lactic acid** (lak′tik as′id) Organic compound formed from pyruvic acid in the anaerobic pathway of cellular respiration.

**lacuna** (lah-ku′nah) Hollow cavity.

**lamella** (lah-mel′ah) Layer of matrix surrounding the central canal of an osteon.

**laryngopharynx** (lah-ring″go-far′ingks) Lower part of the pharynx posterior to the larynx.

**larynx** (lar′inks) Structure superior to the trachea that houses the vocal cords.

**latent period** (la′tent pe′re-od) Time between application of a stimulus and the beginning of a response in a muscle fiber.

**lateral** (lat′er-al) Pertaining to the side.

**leukocyte** (lu′ko-sīt) White blood cell.

**lever** (lev′er) Simple mechanical device consisting of a rod, fulcrum, weight, and a source of energy that is applied to some point on the rod.

**ligament** (lig′ah-ment) Cord or sheet of connective tissue binding two or more bones at a joint.

**limbic system** (lim′bik sis′tem) Connected structures in the brain that produce emotional feelings.

**lingual frenulum** (ling′gwahl fren′u-lum) Fold of tissue that anchors the tongue to the floor of the mouth.

**lipase** (li′pās) Fat-digesting enzyme.

**lipid** (lip′id) Chemical group that includes fats (triglycerides), steroids, and phospholipids.

**lumbar** (lum′bar) Pertaining to the region of the lower back.

**lumen** (lu′men) Space in a tubular structure such as a blood vessel or intestine.

**luteinizing hormone** (lu′te-in-īz″ing hor′mōn) (**LH**) A hormone that the anterior pituitary secretes that controls formation of the corpus luteum in females and testosterone secretion in males.

**lymph** (limf) Fluid carried in lymphatic vessels.

**lymphatic pathway** (lim-fat′ik path′wā) Connected vessels that transport lymph.

**lymph node** (limf nōd) Mass of lymphoid tissue located along the course of a lymphatic vessel.

**lymphocyte** (lim′fo-sīt) Type of white blood cell that provides immunity; B cell or T cell.

**lysosome** (li′so-sōm) Organelle that contains digestive enzymes.

## M

**macromolecule** (mak-rō-mol′ĕ-kūl) Very large molecule, such as protein or nucleic acid.

**macronutrient** (mak-rō-nu′tree-ent) Nutrient (carbohydrate, lipid, and protein) required in large amount.

**macrophage** (mak′ro-fāj) Large phagocytic cell.

**macula lutea** (mak′u-lah lu′te-ah) Yellowish depression in the retina associated with acute vision.

**malnutrition** (mal″nu-trish′un) Symptoms resulting from lack of specific nutrients.

**mammary** (mam′er-e) Pertaining to the breast.

**marrow** (mar′o) Connective tissue in spaces in bones that includes blood-forming stem and progenitor cells.

**mast cell** (mast sel) Cell to which antibodies, formed in response to allergens attach, bursting the cell and releasing allergy mediators, which cause symptoms.

**matter** (mat′er) Anything that has weight and occupies space.

**mechanoreceptor** (mek″ah-no-re-sep′tor) Sensory receptor sensitive to mechanical stimulation, such as changes in pressure or tension.

**medial** (me′de-al) Toward or near the midline.

**mediastinum** (me″de-as-ti′num) Tissues and organs of the thoracic cavity that form a septum between the lungs.

**medulla oblongata** (mĕ-dul′ah ob″long-gah′tah) Part of the brainstem between the pons and the spinal cord.

**medullary cavity** (med′u-lār″e kav′ĭ-te) Cavity containing red or yellow marrow within the diaphysis of a long bone.

**megakaryocyte** (meg″ah-kar′e-o-sīt) Large cell in red bone marrow that fragments to yield blood platelets.

**meiosis** (mi-o′sis) Cell division that halves the genetic material, resulting in egg or sperm.

**melanin** (mel′ah-nin) Dark pigment normally found in skin and hair.

**melanocyte** (mel′ah-no-sīt) Melanin-producing cell.

**melatonin** (mel″ah-to′nin) Hormone that the pineal gland secretes.

**memory cell** (mem′o-re sel) B cell or T cell produced in the primary immune response that can be activated rapidly if the same nonself antigen is encountered in the future.

**menarche** (mĕ-nar′ke) A female's first reproductive cycle.

**meninx** (me′ninks) (plural, *meninges*) Any of the 3 layers of membrane that cover the brain and spinal cord.

**meniscus** (mĕ-nis′kus) (plural, *menisci*) Fibrocartilage that separates the articulating surfaces of bones in the knee.

**menopause** (men′o-pawz) Cessation of the female reproductive cycles.

**merocrine gland** (mer′o-krin gland) A structure whose cells remain intact while secreting; a type of sweat gland.

**mesentery** (mes′en-ter″e) Fold of peritoneal membrane that attaches an abdominal organ to the abdominal wall.

**mesoderm** (mez′o-derm) Middle primary germ layer of the embryo.

**messenger RNA** (mes′in-jer) **(mRNA)** RNA that transmits information for a protein's amino acid sequence from the nucleus to the cytoplasm.

**metabolic pathway** (mĕ-tab′o-lik path-wa) Series of linked, enzymatically controlled chemical reactions.

**metabolism** (mĕ-tab′o-lizm) The combined chemical reactions in cells that use or release energy.

**metacarpal** (met″ah-kar′pal) Bone of the hand between the wrist bones and finger bones.

**metaphase** (met′ah-fāz) Stage in mitosis when chromosomes align in the middle of the cell.

**metatarsal** (met″ah-tar′sal) Foot bone between the ankle bones and the toe bones.

**microfilament** (mi″kro-fil′ah-ment) Rod of actin protein in the cytoplasm that provides structural support or movement. Part of the cytoskeleton.

**microglia** (mi-krog′le-ah) Neuroglia of the CNS that support neurons and phagocytize.

**micronutrient** (mi-kro-nu′tree-ent) Nutrient (vitamins and minerals) required in small amount.

**microtubule** (mi″kro-tu′būl) Hollow rod constructed of many molecules of the protein tubulin. Part of the cytoskeleton.

**microvillus** (mi″kro-vil′us) Tiny, cylindrical process that extends from some epithelial cell membranes, increasing membrane surface area.

**micturition** (mik″tu-rish′un) Urination.

**midbrain** (mid′brān) Small region of the brainstem between the diencephalon and the pons.

**mineral** (min′er-al) Inorganic element essential in human metabolism.

**mineralocorticoid** (min″er-al-o-kor′tĭ-koid) Hormone the adrenal cortex secretes that affects electrolyte concentrations in body fluids.

**mitochondrion** (mi″to-kon′dre-on) (plural, *mitochondria*) Organelle housing enzymes that catalyze the aerobic reactions of cellular respiration.

**mitosis** (mi-to′sis) Division of a somatic cell, forming two genetically identical somatic cells.

**mitral valve** (mi′trul valv) Heart valve between the left atrium and the left ventricle; bicuspid valve.

**mixed nerve** (mikst nerv) Nerve that includes both sensory and motor nerve fibers.

**molecular formula** (mo-lek′u-lar fōr′mu-lah) Abbreviation for the number of atoms of each element in a compound.

**molecule** (mol′ĕ-kūl) Particle composed of two or more joined atoms.

**monocyte** (mon′o-sīt) Type of white blood cell that is a phagocyte.

**monosaccharide** (mon″o-sak′ah-rīd) Simple sugar, such as glucose or fructose.

**motor area** (mo′tor a′re-ah) Region of the brain that sends impulses to muscles or glands.

**motor end plate** (mo′tor end plāt) Specialized part of a muscle fiber membrane at a neuromuscular junction.

**motor nerve** (mo′tor nerv) Nerve that consists of motor nerve fibers.

**motor neuron** (mo′tor nu′ron) Neuron that transmits impulses from the central nervous system to an effector.

**motor speech area** (mo′tor spēch ār′e-ah) Region of the frontal lobe that coordinates complex muscular actions of mouth, tongue, and larynx, making speech possible; Broca's area.

**motor unit** (mo′tor u′nit) A motor neuron and its associated muscle fibers.

**mucosa** (mu-ko′sah) Innermost layer of the alimentary canal.

**mucous cell** (mu′kus sel) Glandular cell that secretes mucus.

**mucous membrane** (mu′kus mem-brān) Membrane that lines cavities and tubes that open to the outside of the body.

**mucus** (mu′kus) Fluid secretion of the mucous cells.

**muscle tissue** (mus′el tish′u) Contractile tissue consisting of filaments of actin and myosin, which slide past each other, shortening cells.

**myelin** (mi′ĕ-lin) Lipid material that forms a sheathlike covering around some axons.

**myelin sheath** (mi′ĕ-lin shēth) Lipid-rich layer formed from certain neuroglia that wraps around an axon, providing insulation.

**myocardium** (mi″o-kar′de-um) Muscle tissue of the heart.

**myofibril** (mi″o-fi′bril) Contractile fiber in muscle cells.

**myoglobin** (mi″o-glo′bin) Pigmented compound in muscle tissue that stores oxygen.

**myometrium** (mi″o-me′tre-um) Layer of smooth muscle tissue in the uterine wall.

**myosin** (mi′o-sin) Protein that, with actin, forms the filaments that interact to contract muscle fibers.

## N

**nasal cavity** (na′zal kav′ĭ-te) Space in the nose.

**nasal concha** (na′zal kong′kah) Shell-like bone extending outward from the wall of the nasal cavity; turbinate bone.

**nasal septum** (na′zal sep′tum) Wall of bone and cartilage that separates the nasal cavity into two parts.

**nasopharynx** (na″zo-far′inks) Part of the pharynx posterior to the nasal cavity.

**negative feedback** (neg′ah-tiv fēd′bak) A mechanism that restores the level of a biochemical or other balance in the internal environment

**neonatal** (ne″o-na′tal) The first four weeks after conception.

**nephron** (nef′ron) Functional unit of a kidney, consisting of renal corpuscle and renal tubule.

**nervous tissue** (ner′vus tish′u) Neurons and neuroglia.

**neurilemma** (nu″rĭ-lem′ah) Sheath formed from Schwann cells on the exterior of some axons.

**neurofibril** (nu″ro-fi′bril) Fine, cytoplasmic thread that extends from the cell body into the processes of a neuron.

**neuroglia** (nu-rog′le-ah) Specialized cells of the nervous system that produce myelin, communicate between cells, maintain the ionic environment, and nurture the differentiation of neurons.

**neuromuscular junction** (nu″ro-mus′ku-lar jungk′shun) Synapse between a motor neuron and a skeletal muscle fiber.

**neuron** (nu′ron) Nerve cell.

**neurotransmitter** (nu″ro-trans′mit-er) Chemical that an axon secretes that stimulates or inhibits an effector (muscle or gland) or other neuron.

**neutral** (nu′tral) Neither acidic nor alkaline; pH7.

**neutron** (nu′tron) Electrically neutral subatomic particle.

**neutrophil** (nu′tro-fil) A type of phagocytic leukocyte.

**nonelectrolyte** (non″e-lek′tro-līt) Substance that does not dissociate into ions when dissolved in water.

**nonprotein nitrogenous substance** (non-pro′te-in ni-troj′ĕ-nus sub′stans) A substance, such as urea or uric acid, that contains nitrogen but is not a protein.

**norepinephrine** (nor″ep-ĭ-nef′rin) Neurotransmitter released from the axons of some nerve cells.

**nuclear envelope** (nu′kle-er ahn-veh-lop) Double membrane surrounding the cell nucleus and separating it from the cytoplasm.

**nucleic acid** (nu-kle′ik as′id) A molecule that is a polymer of nucleotides; RNA or DNA.

**nucleolus** (nu-kle′o-lus) (plural, *nucleoli*) Small structure in the cell nucleus that contains RNA and proteins.

**nucleotide** (nu′kle-o-tīd″) Building block of a nucleic acid molecule, consisting of a sugar, a nitrogenous base, and a phosphate group.

**nucleus** (nu′kle-us) (plural, *nuclei*) The dense core of an atom, composed of protons and neutrons. Cellular organelle enclosed by double-layered, porous membrane and containing DNA. Masses of interneuron cell bodies in the central nervous system.

**nutrient** (nu′tre-ent) Chemical that the body requires from the environment.

## O

**occipital** (ok-sip′ĭ-tal) Pertaining to the lower, back part of the head.

**olfactory** (ol-fak′to-re) Pertaining to the sense of smell.

**olfactory nerves** (ol-fak′to-re nervz) The first pair of cranial nerves, which conduct impulses associated with the sense of smell.

**oligodendrocyte** (ol″ĭ-go-den′dro-sīt) Type of neuroglia that produces myelin in the CNS.

**oocyte** (o′o-sīt) Cell formed by oogenesis. Egg cell.

**oogenesis** (o″o-jen′ĕ-sis) Formation of an oocyte (egg cell).

**optic chiasma** (op′tik ki-az′mah) X-shaped structure on the underside of the brain formed by optic nerve fibers (axons) that partially cross over.

**optic disc** (op′tik disk) Region in the retina where nerve fibers (axons) exit, becoming part of the optic nerve.

**oral** (o′ral) Pertaining to the mouth.

**organ** (or′gan) Structure consisting of a group of tissues with a specialized function.

**organelle** (or″gah-nel′) A structure in a cell that has a specialized function.

**organic** (or-gan′ik) Chemicals that contain both carbon and hydrogen.

**organism** (or′gah-nizm) An individual living thing.

**organ system** (or′gan sis′tem) Group of organs coordinated to carry on a specialized function.

**orgasm** (or′gazm) An intense sensation that is the peak of sexual excitement.

**origin** (or′ĭ-jin) End of a muscle that attaches to a relatively immovable part.

**oropharynx** (o″ro-far′inks) Part of the pharynx posterior to the oral cavity.

**osmosis** (oz-mo′sis) Movement of water through a semipermeable membrane toward a concentration of an impermeant solute.

**osmotic pressure** (oz-mot′ik presh′ur) Pressure needed to stop osmosis; a solution's potential pressure caused by impermeant solute particles in the solution.

**ossification** (os″ĭ-fĭ-ka′shun) Formation of bone tissue.

**osteoblast** (os′te-o-blast″) Bone-forming cell.

**osteoclast** (os′te-o-klast″) Cell that breaks down bone.

**osteocyte** (os′te-o-sīt) Mature bone cell.

**osteon** (os′te-on) Cylinder-shaped unit containing bone cells that surround a central canal; Haversian system.

**oval window** (o′val win′do) Connection between the stapes and the inner ear.

**ovary** (o′var-e) Primary female reproductive organ that produces oocytes.

**ovulation** (o″vu-la′shun) Release of an egg cell from a mature ovarian follicle.

**oxidation** (ok″sĭ-da′shun) Process by which oxygen combines with another chemical; removal of hydrogen or the loss of electrons; opposite of reduction.

**oxygen debt** (ok′sĭ-jen det) Amount of oxygen required following physical exercise to react accumulated lactic acid to form glucose.

**oxyhemoglobin** (ok″sĭ-he″mo-glo′bin) Compound formed when oxygen binds to hemoglobin.

**oxytocin** (ok″sĭ-to′sin) Hormone released by the posterior pituitary that contracts smooth muscles in the uterus and mammary glands.

## P

**pacemaker** (pās′māk-er) Mass of specialized cardiac muscle tissue that controls the rhythm of the heartbeat; sinoatrial node.

**pain receptor** (pān re″sep′tor) Sensory nerve ending that transmits impulses interpreted as pain.

**palate** (pal′at) Roof of the mouth.

**palatine** (pal′ah-tīn) Pertaining to the palate.

**palmar** (pahl′mar) Pertaining to the palm of the hand.

**pancreas** (pan′kre-as) Glandular organ in the abdominal cavity that secretes hormones and digestive enzymes.

**pancreatic juice** (pan″kre-at′ik jo͞os) Digestive secretions of the pancreas.

**papilla** (pah-pil′ah) Tiny, nipplelike projection.

**papillary muscle** (pap′ĭ-ler″e mus′l) Muscle that extends inward from the ventricular walls of the heart and to which the chordae tendineae attach.

**paranasal sinus** (par″ah-na′zal si-nus) Air-filled cavity in a cranial or facial bone lined with mucous membrane and connected to the nasal cavity.

**parasympathetic division** (par″ah-sim″pah-thet′ik de-vijh′in) Part of the autonomic nervous system that arises from the brain and sacral region of the spinal cord.

**parathyroid gland** (par″ah-thi′roid gland) One of four small endocrine glands embedded in the posterior part of the thyroid gland.

**parathyroid hormone** (par″ah-thi′roid hor′mōn) **(PTH)** Hormone secreted by the parathyroid glands that helps regulate the levels of blood calcium and phosphate ions.

**parietal** (pah-ri′ĕ-tal) Pertaining to the wall of a cavity.

**parietal cell** (pah-ri′ĕ-tal sel) Cell of a gastric gland that secretes hydrochloric acid and intrinsic factor.

**parietal pericardium** (pah-ri′ĕ-tal per″ĭ-kar′de-um) Membrane that forms the outer wall of the pericardial cavity.

**parietal peritoneum** (pah-ri′ĕ-tal per″ĭ-to-ne′-um) Membrane that forms the outer wall of the peritoneal cavity.

**parietal pleura** (pah-ri′ĕ-tal ploo′rah) Membrane that forms the outer wall of the thoracic cavity.

**parotid gland** (pah-rot′id gland) Large salivary gland on the side of the face just in front and below the ear.

**partial pressure** (par′shal presh′ur) Pressure one gas produces in a mixture of gases.

**pathogen** (path′o-jen) Disease-causing agent.

**pectoral** (pek′tor-al) Pertaining to the chest.

**pectoral girdle** (pek′tor-al ger′dl) Part of the skeleton that supports and attaches the upper limbs.

**pedigree** (ped′eh-gree) Chart that displays relationships among family members and their inherited traits and disorders.

**pelvic cavity** (pel′vik kav′ĭ-te) Hollow place within the ring formed by the sacrum and hip bones that encloses the terminal part of the large intestine, the urinary bladder, and the internal reproductive organs.

**pelvic girdle** (pel′vik ger′dl) Part of the skeleton to which the lower limbs attach.

**pelvis** (pel′vis) Bony ring formed by the sacrum and hip bones (bony pelvis); the pelvic cavity.

**penis** (pe′nis) Male external reproductive organ through which the urethra passes.

**pepsin** (pep′sin) Protein-splitting enzyme that the gastric glands secrete.

**pepsinogen** (pep-sin′o-jen) Inactive form of pepsin.

**pericardial cavity** (per″ĭ-kar′de-al kav′ĭ-te) Potential space between the visceral and parietal pericardial membranes.

**pericardium** (per″ĭ-kar′de-um) Serous membrane that surrounds the heart.

**perichondrium** (per″ĭ-kon′dre-um) Layer of dense connective tissue that encloses cartilaginous structures.

**perilymph** (per′ĭ-limf) Fluid in the space between the membranous and osseous labyrinths of the inner ear.

**perimetrium** (per-ĭ-me′tre-um) Outer serosal layer of the uterine wall.

**perimysium** (per″i-mis′e-um) Sheath of connective tissue that encloses a bundle of skeletal muscle fibers.

**periodontal ligament** (per″e-o-don′tal lig′ah-ment) Fibrous membrane around a tooth that attaches it to the jawbone.

**periosteum** (per″e-os′te-um) Dense connective tissue covering the surface of a bone.

**peripheral nervous system** (pĕ-rif′er-al ner′vus sis′tem) **(PNS)** Parts of the nervous system outside the central nervous system.

**peripheral resistance** (pĕ-rif′er-al re-zis′tans) Combined peripheral resistance to blood flow due to friction between the blood and blood vessel walls.

**peristalsis** (per″ĭ-stal′sis) Rhythmic waves of muscular contraction in the walls of certain tubular organs.

**peritoneal cavity** (per″ĭ-to-ne′al kav′ĭ-te) Potential space between the visceral and parietal peritoneal membranes.

**peritubular capillary** (per″ĭ-tu′bu-lar kap′ĭ-ler″e) Capillary that surrounds a renal tubule and functions in tubular reabsorption and tubular secretion during urine formation.

**peroxisome** (pĕ-roks′ĭ-sōm) Membranous sac abundant in kidney and liver cells that contains enzymes that catalyze reactions that decompose hydrogen peroxide.

**pH** (pH) A shorthand system that indicates the acidic or alkaline condition of a solution; values range from 0 to 14. Technically the negative log of the hydrogen ion concentration.

**phagocytosis** (fag″o-si-to′sis) Process by which a cell engulfs and digests solids.

**phalanx** (fa′langks) (plural, *phalanges*) Bone of a finger or toe.

**pharynx** (far′inks) Part of the digestive tube posterior to the nasal and oral cavities, as well as the larynx.

**phenotype** (fe′no-tīp) The expression of a gene or genes.

**pheomelanin** (fe″o-mel′ah-nīn) A reddish-yellow pigment.

**phospholipid** (fos″fo-lip′id) Molecule consisting of two fatty acid molecules and a phosphate group bound to a glycerol molecule.

**photoreceptor** (fo″to-re-sep′tor) Sensory receptor sensitive to light energy; rods and cones of the eyes.

**physiology** (fiz″e-ol′o-je) The study of body functions.

**pia mater** (pi′ah ma′ter) Inner layer of meninges that encloses the brain and spinal cord.

**pineal gland** (pin′e-al gland) A small structure in the central brain that secretes the hormone melatonin, which controls certain biological rhythms.

**pinocytosis** (pi″no-si-to′sis) Process by which a cell engulfs droplets of fluid from its surroundings.

**pituitary gland** (pĭ-tu′ĭ-tār″e gland) Endocrine gland attached to the base of the brain consisting of anterior and posterior lobes.

**placenta** (plah-sen′tah) Structure that attaches the fetus to the uterine wall, delivering nutrients to and removing wastes from the fetus.

**plantar** (plan′tar) Pertaining to the sole of the foot.

**plasma** (plaz′mah) Fluid portion of the blood.

**plasma cell** (plaz′mah sel) Antibody-producing cell that forms when activated B cells proliferate.

**plasma protein** (plaz′mah pro′te-in) Protein dissolved in blood plasma.

**platelet** (plāt′let) Cellular fragment formed in red bone marrow that helps blood clot.

**pleural cavity** (ploo′ral kav′ĭ-te) Potential space between pleural membranes.

**pleural membrane** (ploo′ral mem′brān) Serous membrane that encloses the lungs and lines the chest wall.

**plexus** (plek′sus) Network of interlaced nerves or blood vessels.

**polar body** (pō′lar bod′e) Small, nonfunctional cell that is a product of meiosis in the female.

**polarization** (po″lar-ĭ-za′shun) Voltage difference across a cell membrane due to an unequal distribution of positive and negative ions on either side of the membrane.

**polysaccharide** (pol″e-sak′ah-rīd) Carbohydrate composed of many joined monosaccharides.

**polyunsaturated fatty acid** (pol″e-un-sach′ĕ-ra-ted fat′e as′id) Fatty acid with more than one double carbon bond.

**pons** (ponz) Part of the brainstem above the medulla oblongata and below the midbrain.

**popliteal** (pop″lĭ-te′al) Pertaining to the region behind the knee.

**positive feedback system** (poz′ĭ-tiv fēd′bak sis′tem) Process by which changes cause additional similar changes, producing unstable conditions.

**posterior** (pos-tēr′e-or) Toward the back; the opposite of *anterior.*

**posterior pituitary** (pos-tēr′e-or pĭ-tu′ĭ-tār″e) The lobe of the pituitary gland that secretes oxytocin and antidiuretic hormone (vasopressin).

**postganglionic fiber** (pōst″gang-gle-on′ik fi′ber) Axon of an autonomic neuron on the distal side of a ganglion.

**postnatal** (pōst-na′tal) After birth.

**preganglionic fiber** (pre″gang-gle-on′ik fi′ber) Axon of an autonomic neuron on the proximal side of a ganglion.

**pregnancy** (preg′nan-se) Condition in which a female has a developing offspring in her uterus.

**prenatal** (pre-na′tal) Before birth.

**primary follicle** (pri′ma-re fol′ĭ-kl) Primordial follicle that begins to mature in response to hormonal changes in a female.

**primary germ layers** (pri′mar-e jerm la′erz) Three layers of cells in the embryo that divide and differentiate into specific tissues and organs; ectoderm, mesoderm, and endoderm.

**primary sex organs** (pri′ma-re seks or′ganz) Sex-cell-producing parts; testes in males and ovaries in females.

**prime mover** (prīm moov′er) Muscle that provides most of a particular body movement. Also called an agonist.

**progenitor cell** (pro-jen′ĭ-tor sel) Daughter cell of a stem cell whose own daughter cells are restricted to follow specific lineages.

**progesterone** (pro-jes′tĭ-rōn) Female hormone secreted by the corpus luteum and placenta.

**projection** (pro-jek′shun) Process by which the brain causes a sensation to seem to come from the region of the body being stimulated.

**prolactin** (pro-lak′tin) **(PRL)** Hormone secreted by the anterior pituitary that stimulates milk production in the mammary glands.

**pronation** (pro-na′shun) Downward or inward rotation of the palm.

**prophase** (pro′fāz) Stage of mitosis when chromosomes become visible when stained and viewed under a microscope.

**prostaglandins** (pros″tah-glan′dins) A group of compounds with powerful, hormonelike effects.

**prostate gland** (pros′tāt gland) Gland surrounding the male urethra below the urinary bladder that secretes into semen prior to ejaculation.

**protein** (pro′tēn) Nitrogen-containing organic compound consisting of bonded amino acid molecules.

**prothrombin** (pro-throm′bin) Plasma protein that functions in blood clotting.

**proton** (pro′ton) Positively charged particle in an atomic nucleus.

**protraction** (pro-trak′shun) Forward movement of a body part.

**proximal** (prok′sĭ-mal) Closer to the point of attachment; opposite of *distal.*

**pseudostratified columnar epithelium** (soo″do-strat′ĭ-fīd co-lum′nar ep″ĭ-the′lē-um) Single layer of cells appearing as more than one layer because the nuclei occupy different positions in the cells.

**PTH** Parathyroid hormone.

**puberty** (pu′ber-te) Stage of development in which the reproductive organs become functional.

**pubic** (pu′bik) Region between the left and right inguinal regions.

**pulmonary circuit** (pul′mo-ner″e ser′kit) System of blood vessels that carries blood between the heart and the lungs.

**pulse** (puls) Surge of blood felt through the walls of arteries due to the contraction of the heart ventricles.

**Punnett square** (pun-it sqware) A grid diagram that displays possible progeny that can be predicted based on parental gametes.

**pupil** (pu′pil) Opening in iris through which light enters the eye.

**Purkinje fibers** (pur-kin′je fi′berz) Specialized cardiac muscle fibers that conduct cardiac impulses from the AV bundle into the ventricular walls.

**pyruvic acid** (pi-roo′vik as′id) Intermediate product of carbohydrate oxidation.

## R

**radioactive** (ra″de-o-ak′tiv) Property of some atoms that releases energy at a constant rate.

**rate-limiting enzyme** (rāt lim′i-ting en′zīm) Enzyme, usually present in small amounts, that controls the rate of a metabolic pathway by regulating one step.

**receptor** (re-sep′tor) Specialized cell that provides information about the environment. Also, cell membrane protein that binds specific molecules, called ligands, thereby sending a signal inside the cell.

**recessive** (re-sess′iv) A gene whose expression is masked by another (dominant).

**recruitment** (re-kro͞ot′ment) Increase in the number of motor units activated as stimulation intensity increases.

**red marrow** (red mar′o) Blood-cell-forming tissue in spaces within bones.

**referred pain** (re-ferd′ pān) Pain that feels as if it is originating from a part other than the site being stimulated.

**reflex** (re′fleks) A rapid, automatic response to a stimulus.

**reflex arc** (re′fleks ark) Nerve pathway, consisting of a sensory receptor, a sensory neuron, interneuron, motor neuron, and an effector that forms the structural and functional bases for a reflex.

**refraction** (re-frak′shun) Bending of light as it passes between media of different densities.

**relaxin** (re-lak′sin) Hormone from the corpus luteum that inhibits uterine contractions during pregnancy.

**renal corpuscle** (re′nal kor′pusl) Part of a nephron that consists of a glomerulus and a glomerular capsule.

**renal cortex** (re′nal kor′teks) Outer part of a kidney.

**renal medulla** (re′nal mĕ-dul′ah) Inner part of a kidney.

**renal pelvis** (re′nal pel′vis) Cavity in a kidney that channels urine to the ureter.

**renal tubule** (re′nal tu′būl) Part of a nephron that extends from the renal corpuscle to the collecting duct.

**renin** (re′nin) Enzyme that kidneys release that maintains blood pressure and blood volume.

**replication** (rep″lĭ-ka′shun) Copying of a DNA molecule.

**respiration** (res″pĭ-ra′shun) Breathing.

**respiratory capacity** (re-spi′rah-to″re kah-pas′ĭ-te) The sum of any two or more respiratory volumes.

**respiratory membrane** (re-spi′rah-to″re mem′brān) Membrane composed of a capillary wall, an alveolar wall, and their basement membranes through which blood and inspired air exchange gases.

**resting potential** (res′ting po-ten′shal) Difference in electrical charge between the inside and the outside of an undisturbed nerve cell membrane.

**reticular fiber** (rĕ-tik′u-lar fi′ber) Thin collagenous fiber.

**reticular formation** (rĕ-tik′u-lar for-ma′shun) Complex network of nerve fibers in the brainstem that arouses the cerebrum.

**retina** (ret′ĭ-nah) Inner layer of the eye wall that includes the visual receptors.

**retraction** (rĕ-trak′shun) Movement of a part toward the back.

**retroperitoneal** (ret″ro-per″i-to-ne′al) Behind the peritoneum.

**reversible reaction** (re-ver′sĭ-bl re-ak′shun) Chemical reaction in which the products react, reforming the reactants.

**rhodopsin** (ro-dop′sin) Light-sensitive pigment in the rods of the retina; visual purple.

**ribonucleic acid** (ri″bo-nu-kle′ik as′id) **(RNA)** Single stranded polymer of nucleotides in which each nucleotide includes the sugar ribose, a phosphate group, and a nitrogenous base (adenine, uracil, guanine, or cytosine).

**ribosome** (ri′bo-sōm) Organelle composed of RNA and protein that is a structural support for protein synthesis.

**RNA** Ribonucleic acid.

**rod** (rod) Type of light receptor that provides colorless (black and white) vision.

**rotation** (ro-ta′shun) Movement turning a body part on its longitudinal axis.

**round window** (rownd win′do) Membrane-covered opening between the inner ear and the middle ear.

## S

**saccule** (sak′ ūl) An enlarged region of the membranous labyrinth of the inner ear.

**sagittal** (saj′ĭ-tal) Plane or section that divides a structure into right and left portions.

**salivary amylase** (sal′i-ver-e am′i-lās) Enzyme that hydrolyzes (digests) starch in the mouth.

**salt** (salt) Compound produced by the reaction of an acid and a base.

**SA node** (nōd) Sinoatrial node.

**sarcomere** (sar′ko-mēr) Structural and functional unit of a myofibril.

**sarcoplasmic reticulum** (sar″ko-plaz′mik rĕ-tik′u-lum) Membranous network of channels and tubules of a muscle fiber, corresponding to the endoplasmic reticulum of other cells.

**saturated fatty acid** (sat′u-rāt″ed fat′e as′id) Fatty acid molecule that includes maximal hydrogens and therefore has no double carbon bonds.

**Schwann cell** (shwahn sel) Type of neuroglia that surrounds an axon of a peripheral neuron, forming the myelin-rich neurilemmal sheath and myelin.

**sclera** (skle′rah) White, fibrous outer layer of the eyeball.

**scrotum** (skro′tum) Pouch of skin that encloses the testes.

**sebaceous gland** (se-ba′shus gland) Skin gland that secretes sebum.

**sebum** (se′bum) Oily secretion of sebaceous glands.

**secretin** (se-kre′tin) Hormone from the small intestine that stimulates the pancreas to release pancreatic juice.

**selectively permeable** (se-lek′tiv-le per′me-ah-bl) Membrane that allows some types of molecules through but not others; semipermeable.

**semen** (se′men) Fluid containing sperm cells and secretions discharged from the male reproductive tract at ejaculation.

**semicircular canal** (sem″ĭ-ser′ku-lar kah-nal′) Tubular structure in the inner ear that houses receptors providing the sense of dynamic equilibrium.

**seminiferous tubule** (sem″ĭ-nif′er-us tu′būl) Tubule in the testes where sperm cells form.

**sensation** (sen-sa′shun) A feeling resulting from the brain's interpretation of sensory impulses.

**sensory area** (sen′so-re a′re-ah) Part of the cerebral cortex that receives and interprets sensory impulses.

**sensory nerve** (sen′so-re nerv) A nerve composed of sensory nerve fibers.

**sensory neuron** (sen′so-re nu′ron) Neuron that transmits impulses from sensory receptors to the central nervous system.

**sensory receptor** (sen′so-re re″sep′tor) Specialized structure associated with the peripheral end of a sensory neuron specific to detecting a particular sensation and triggering an impulse in response.

**sensory speech area** (sen′so-re spēch ār′e-ah) Region of the parietal lobe and the temporal lobe just posterior to the lateral sulcus that is necessary for understanding written and spoken language; Wernicke's area.

**serosa** (sĕ′ro-sah) Outer covering of the alimentary canal.

**serotonin** (se″ro-to′nin) Vasoconstrictor released from blood platelets when blood vessels break, controlling bleeding. Also a neurotransmitter.

**serous cell** (ser′us sel) Glandular cell that secretes a watery fluid (serous fluid) with high enzyme content.

**serous membrane** (ser′us mem′brān) Membrane that lines a cavity that does not open to the outside of the body.

**set point** (set′ point) Target value of a physiological condition maintained in the body by homeostasis.

**sex chromosome** (seks crō-mo-some) Chromosome that carries genes responsible for the development of characteristics associated with maleness or femaleness; an X or Y chromosome.

**simple sugar** (sim′pl shoog′ar) Monosaccharide.

**sinoatrial node** (si″no-a′tre-al nōd) **(SA node)** Specialized tissue in the wall of the right atrium that initiates cardiac cycles; pacemaker.

**skeletal muscle tissue** (skel′ĭ-tal mus′l tish′u) Type of voluntary muscle tissue in muscles attached to bones.

**smooth muscle tissue** (smooth mus′l tish′u) Type of involuntary muscle tissue.

**solute** (sol′ūt) Chemical dissolved in a solution.

**solvent** (sol′vent) Liquid portion of a solution in which a solute is dissolved.

**somatic nervous system** (so-mat′ik ner′vus sis′tem) Motor pathways of the peripheral nervous system that lead to skeletal muscles.

**special sense** (spesh′al sens) Sense that stems from receptors associated with specialized sensory organs, such as the eyes and ears.

**spermatid** (sper′mah-tid) Intermediate stage in sperm cell formation.

**spermatogenesis** (sper″mah-to-jen′ĕ-sis) Sperm cell production.

**spermatogonium** (sper″mah-to-go′ne-um) Undifferentiated spermatogenic cell in the outer part of a seminiferous tubule.

**spinal cord** (spi′nal kord) Part of the central nervous system extending from the brainstem below the foramen magnum through the vertebral canal.

**spinal nerve** (spi′nal nerv) Nerve that arises from the spinal cord.

**spleen** (splēn) Large organ in the upper left region of the abdomen that is a blood reservoir.

**spongy bone** (spun′jē bōn) Bone that consists of bars and plates separated by irregular spaces; cancellous bone.

**static equilibrium** (stat′ik e″kwĭ-lib′re-um) Maintenance of balance when the head and body are motionless.

**stem cell** (stem sel) Undifferentiated cell that can divide to yield two daughter stem cells, or a stem cell and a progenitor cell.

**steroid** (ste′roid) Type of lipid including complex rings of carbon and hydrogen atoms.

**stomach** (stum′ak) Digestive organ between the esophagus and small intestine.

**stratum basale** (strat′tum ba′sal-e) Deepest layer of the epidermis, where cells divide; stratum germinativum.

**stratum corneum** (stra′tum kor′ne-um) Outer, horny layer of the epidermis.

**stressor** (stres′or) Factor capable of stimulating a stress response.

**stroke volume** (strōk vol′ūm) Volume of blood the ventricle discharges with each heartbeat.

**structural formula** (struk′cher-al for′mu-lah) Representation of the way atoms bond to form a molecule, using symbols for each element and lines to indicate chemical bonds.

**subarachnoid space** (sub″ah-rak′noid spās) Space in the meninges between the arachnoid mater and the pia mater.

**subcutaneous layer** (sub″ku-ta′ne-us la′yer) Loose connective tissue layer that is mostly fat and beneath the skin.

**sublingual** (sub-ling′gwal) Beneath the tongue.

**submucosa** (sub″mu-ko′sah) Layer of the alimentary canal underneath the mucosa.

**substrate** (sub′strāt) Target of enzyme action.

**sucrase** (su′krās) Digestive enzyme that catalyzes the breakdown of sucrose.

**sulcus** (sul′kus) (plural, *sulci*) Shallow groove, such as that between gyri on the brain surface.

**summation** (sum-ma′shun) Increased force of contraction by a skeletal muscle fiber when a twitch occurs before the previous twitch relaxes.

**superior** (soo-pe′re-or) Structure above another structure.

**surface tension** (sur′fis ten′shun) Force that adheres moist membranes due to the attraction of water molecules.

**surfactant** (ser-fak′tant) Substance produced by the lungs that reduces the surface tension in alveoli.

**sweat gland** (swet gland) Exocrine gland in skin that secretes a mixture of water, salt, urea, and other bodily substances.

**sympathetic nervous system** (sim″pah-thet′ik ner′vus sis′tem) Part of the autonomic nervous system that arises from the thoracic and lumbar regions of the spinal cord.

**synapse** (sin′aps) Functional connection between the axon of a neuron and the dendrite or cell body of another neuron or the membrane of another cell type.

**synaptic cleft** (sĭ-nap′tik kleft) Space between two cells forming a synapse.

**synaptic knob** (sĭ-nap′tik nob) Tiny enlargement at the end of an axon that secretes a neurotransmitter.

**synergist** (sin′er-jist) Muscle that assists the action of an agonist.

**synovial joint** (sĭ-no′ve-al joint) Freely movable joint.

**synovial membrane** (sĭ-no′ve-al mem′brān) Membrane that forms the inner lining of the capsule of a freely movable joint.

**synthesis** (sin′thĕ-sis) Building large molecules from smaller ones.

**systemic circuit** (sis-tem′ik ser′kit) Vessels that conduct blood between the heart and all body tissues except the lungs.

**systole** (sis′to-le) Phase of the cardiac cycle when a heart chamber wall contracts.

**systolic pressure** (sis-tol′ik presh′ur) Arterial blood pressure reached during the systolic phase of the cardiac cycle.

## T

**target cell** (tar′get sel) Cell with specific receptors on which a hormone exerts its effect.

**tarsal** (tahr′sul) Ankle bone.

**taste bud** (tāst bud) Organ containing receptors associated with the sense of taste.

**T cell** (sel) A type of lymphocyte that interacts directly with antigens, producing the cellular immune response.

**telophase** (tel′o-fāz) Stage in mitosis when newly formed cells separate.

**tendon** (ten′don) Cordlike or bandlike mass of white fibrous connective tissue that connects a muscle to a bone.

**testis** (tes′tis) (plural, *testes*) Primary male reproductive organ; sperm-cell-producing organ.

**testosterone** (tes-tos′tĕ-rōn) Male sex hormone secreted by the interstitial cells of the testes.

**tetanic contraction** (tĕ-tan′ik kon-trak′shun) Continuous, forceful muscular contraction without relaxation.

**thalamus** (thal′ah-mus) Mass of gray matter at the base of the cerebrum in the wall of the third ventricle.

**thermoreceptor** (ther″mo-re-sep′tor) Sensory receptor sensitive to temperature changes; heat and cold receptors.

**thoracic cavity** (tho-ras′ik kav′ĭ-te) Hollow space inside the chest containing the thoracic organs.

**threshold potential** (thresh′old po-ten′shul) Stimulation level that must be exceeded to elicit an action potential or a muscle contraction.

**thrombus** (throm′bus) Blood clot that remains where it forms in a blood vessel.

**thymosins** (thi′mo-sinz) Group of peptides the thymus secretes that increases production of certain types of white blood cells.

**thymus** (thī′mus) Glandular organ in the mediastinum behind the sternum and between the lungs.

**thyroid gland** (thi′roid gland) Endocrine gland located just below the larynx and in front of the trachea that secretes thyroid hormones.

**thyroid-stimulating hormone** (thi-roid stim-ū-lay-ting hor-mone) **(TSH)** Hormone secreted from the anterior pituitary that controls secretion from the thyroid gland.

**thyroxine** (thi-rok′sin) Hormone secreted by the thyroid gland; T4.

**tissue** (tish′u) Group of similar cells that performs a specialized function.

**trachea** (tra′ke-ah) Tubular organ that leads from the larynx to the bronchi.

**transcellular fluid** (trans″sel′u-lar floo′id) Part of the extracellular fluid; includes the fluid within special body cavities.

**transcription** (trans-krip′shun) Manufacturing a complementary RNA from DNA.

**transfer RNA** (trans′fer) **(tRNA)** RNA molecule that carries an amino acid to a ribosome in protein synthesis.

**translation** (trans-la′shun) Assembly of an amino acid chain according to the sequence of base triplets in an mRNA molecule.

**transverse** (tranz-vers′) Plane that divides a structure into superior and inferior portions.

**transverse tubule** (trans-vers′ tu′būl) Membranous channel that extends inward from a muscle fiber membrane.

**tricuspid valve** (tri-kus′pid valv) Heart valve between the right atrium and the right ventricle.

**triglyceride** (tri-glis′er-īd) Lipid composed of three fatty acids and a glycerol molecule; a fat or oil.

**triiodothyronine** (tri″i-o″do-thi′ro-nēn) Type of thyroid hormone; T3.

**trypsin** (trip′sin) Enzyme in pancreatic juice that breaks down protein molecules.

**twitch** (twich) Single contraction of a muscle fiber followed by relaxation.

## U

**umbilical cord** (um-bil′ĭ-kal kord) Cordlike structure, containing one vein and two arteries, that connects the fetus to the placenta.

**umbilical region** (um-bil′ĭ-kal re′jun) Central portion of the abdomen.

**unsaturated fatty acid** (un-sat′u-rāt″ed fat′e as′id) Fatty acid molecule with one or more double carbon bonds.

**urea** (u-re′ah) Nonprotein nitrogenous substance resulting from protein metabolism.

**ureter** (u-re′ter) Muscular tube that carries urine from the kidney to the urinary bladder.

**urethra** (u-re′thrah) Tube leading from the urinary bladder to the outside of body.

**urine** (u′rin) Wastes and excess water and electrolytes removed from the blood and excreted by the kidneys into the ureters, to the urinary bladder, and out of the body through the urethra.

**uterine tube** (u′ter-in tūb) Tube that extends from the uterus on each side toward an ovary and transports sex cells; oviduct or Fallopian tube.

**uterus** (u′ter-us) Hollow, muscular organ in the female pelvis where a fetus develops.

**utricle** (u′trĭ-kl) Enlarged part of the membranous labyrinth of the inner ear.

**uvula** (u′vu-lah) Fleshy part of the soft palate that extends down above the root of the tongue.

## V

**vaccine** (vak′sēn) Preparation that includes antigens that stimulate an immune response to prevent an infectious disease.

**vagina** (vah-ji′nah) Tubular organ that leads from the uterus to the vestibule of the female reproductive tract.

**vasoconstriction** (vas″o-kon-strik′shun) Decrease in the diameter of a blood vessel.

**vasodilation** (vas″o-di-la′shun) Increase in the diameter of a blood vessel.

**vein** (vān) Vessel that carries blood toward the heart.

**vena cava** (ve′nah kav′ah) One of two large veins (superior and inferior) that convey deoxygenated blood to the right atrium of the heart.

**ventral root** (ven′tral root) Motor branch of a spinal nerve by which it connects with the spinal cord.

**ventricle** (ven′trĭ-kl) Cavity, such as a brain ventricle filled with cerebrospinal fluid, or heart ventricle that contains blood.

**venule** (ven′ūl) Vessel that carries blood from capillaries to a vein.

**vertebral** (ver′te-bral) Pertaining to the bones of the spinal column.

**vesicle** (ves′ĭ-kal) Membranous cytoplasmic sac formed by an infolding of the cell membrane or pinching off of membranes within the cell.

**viscera** (vis′er-ah) Organs in a body cavity.

**visceral pericardium** (vis′er-al per″ĭ-kar′de-um) Membrane that covers the surface of the heart.

**visceral peritoneum** (vis′er-al per″ĭ-to-ne′-um) Membrane that covers organ surfaces in the abdominal cavity.

**visceral pleura** (vis′er-al ploo′rah) Membrane that covers the surfaces of the lungs.

**viscosity** (vis-kos′ĭ-te) Tendency for a fluid to resist flowing due to the internal friction of its molecules.

**vitamin** (vi′tah-min) Organic compound other than carbohydrate, lipid, or protein needed for normal metabolism that the body cannot synthesize in adequate amounts and must therefore be obtained in the diet.

**vitreous humor** (vit′re-us hu′mor) Fluid between the lens and the retina of the eye.

**vocal cord** (vo′kal kord) Fold of tissue of the larynx that produces sound when it vibrates.

**vulva** (vul′vah) External female reproductive parts that surround the vaginal opening.

## W

**water balance** (wot′er bal′ans) When the volume of water entering the body is equal to the volume leaving it.

**water of metabolism** (wot′er uv mĕ-tab′o-lizm) Water produced as a by-product of aerobic metabolism.

## Y

**yellow marrow** (yel′o mar′o) Fat storage tissue in certain bone cavities.

## Z

**zygote** (zi′gōt) Cell produced when an egg and a sperm fuse; fertilized ovum.

**zymogen granule** (zi-mo′jen gran′ūl) Cellular structure that stores inactive forms of protein-splitting enzymes in a pancreatic cell.

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